

POCKET ICU

GYORGY FRENDL RICHARD D. URMAN

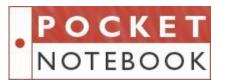
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Pocket I C U



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business Two Commerce Square 2001 Market Street Philadelphia, PA 19103 USA LWW.com

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Printed in China

Library of Congress Cataloging-in-Publication Data

Pocket ICU / [edited by] Gyorgy Frendl, Richard D. Urman.

p.; cm. – (Pocket notebook series)

Includes bibliographical references and index.

ISBN 978-1-4511-0984-9 (alk. paper)

I. Frendl, Gyorgy. II. Urman, Richard D. III. Series: Pocket notebook. [DNLM: 1. Intensive Care—methods—Handbooks. 2. Individualized Medicine—Handbooks. 3. Intensive Care Units—Handbooks. WX 39]

616.02'8-dc23

2012010729

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PREFACE

Critical care has always been a multi-disciplinary specialty. The multidisciplinary nature is practiced two ways: (a) critical care integrates knowledge and practices from many medical specialties (trauma, transplant medicine, cardiology, pulmonary medicine, anesthesiology and pain medicine, and many others); and (b) it requires the close collaboration of medical professionals from many specialties (nurses, physico-therapists, respiratory therapists, nutritionists, pharmacists, physicians, etc.). For that, critical care professionals are required to be masters of communication, team building, and management.

Since its inception in the polio era (1950s), critical care has grown beyond adolescence and now is considered to be an evidence-based specialty. Dozens of high-quality clinical trials built a solid scientific foundation for critical care, and allowed us to significantly improve both patient survival and quality of life following critical illness. Our mission was to highlight these for our readers.

As we reach for personalized (individualized) medicine to custom tailor our management for every one of our patients, provide care for the elderly in their 80s and 90s, treat diseases that were untreatable just years before, the knowledge has to be solid and the commitment firm that critical care professionals will always put their patients first. The challenges remaining are substantial and will require a well-trained, collaborative, patient-centered and cost-effective effort from all of us.

This book is intended to provide concise, evidence-based information for all critical care professionals, as well as for those who are having their first encounter with ICUs and critically ill patients. To accomplish our goals, we were joined by many leading critical care specialists. We are grateful for their contribution and for sharing their many years of experience.

The rewards of providing care for the most needy are great. With our book, we invite all of you for a great and satisfying professional journey.

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COMMON ICU PROBLEMS

RAGHU SEETHALA, MD

Hyperkalemia

Serum K > 5.0 mmol/l, severe hyperkalemia > 6.0 mmol/l (also see Chapter 6)

Causes

- Renal insufficiency
- Adrenal insufficiency
- Insulin deficiency
- Tissue damage from rhabdomyolysis, trauma, or burns
- Medication related
- Acidosis

Clinical Manifestations

- Peaked T waves on ECG; hyperkalemia depolarizes cardiac membrane leading to further EKG changes, like widening of QRS (sinusoidal wave forms) which can progress to asystole or ventricular fibrillation
- Muscular effects can include paresthesias, weakness, or flaccid paralysis

Management

- Stabilize cardiac membrane
 - Calcium Gluconate (10%) 10 ml IV push over 2–3 min, can repeat q5min
- Shift potassium intracellularly
 - Insulin (regular) 10 U IV push with 25 g of Dextrose IV push (if not hyperglycemic)
 - Albuterol 15–20 mg (beta-agonist) nebulized over 10 min
 - Sodium Bicarbonate 50 mmol IV push or 150 mmol/l IV at a variable rate (only use if patient has a severe metabolic acidosis)
- Potassium elimination from body
 - Furosemide (Lasix) 40-80 mg IV push
 - Sodium polystyrene sulfonate (Kayexalate) 15–30 g in 15–30 ml (70% sorbitol PO)
 - Do not administer in ileus or bowel obstruction because of risk of colonic necrosis
 - Hemodialysis (if hyperkalemia is unresponsive to conservative measures listed above)

SHOCK

Hypoperfusion causing tissue hypoxia resulting in multiorgan dysfunction (also see Chapter 10 for septic and Chapter 27 for cardiogenic shock).

Differential Diagnosis

- Hypovolemic
 - Hemorrhage (trauma, GI bleed, retroperitoneal bleed)
 - Dehydration (vomiting, diarrhea, GI fistula)
 - Third spacing (burns, malnutrition, SIRS)
- Cardiogenic
 - Myocardial infarction
 - Myocarditis
 - End stage cardiomyopathy
 - Valvular failure
 - Congestive heart failure
 - Arrhythmia
- Distributive
 - Sepsis
 - Anaphylaxis
 - Liver failure
 - Neurogenic
 - Adrenal insufficiency
 - Drugs
- Obstructive
 - Tension pneumothorax
 - Cardiac tamponade
 - Constrictive pericarditis
 - Pulmonary embolism
 - Aortic coarctation

Clinical Manifestations

- Hypotension
- Tachycardia
- Tachypnea
- Mottled skin
- Cool extremities
- Altered mental status
- Decreased urine output

Management

- Establish and maintain ABCs (airway, breathing, circulation)
- Fluid resuscitation
- Blood and blood product transfusion
- Vasopressors
- Inotropes
- Hemodynamic monitoring (CVC, arterial line, PA catheter, echocardiogram)
- Consider the following resuscitation endpoints for septic shock (the most common type of shock)
 - CVP 8–12 mm Hg, 12–15 mm Hg if mechanically ventilated
 - MAP \geq 65 mm Hg

- $UOP \ge 0.5 \text{ ml/kg/hr}$
- $ScVO_2 \ge 70\%$ or $MVO_2 \ge 65\%$
- Lactate clearance
- Identification and treatment of underlying problem including source control in septic shock

SEPSIS

Infection associated with a systemic inflammatory response (also see Chapter 10).

Causes

- Pneumonia
- Catheter-related blood stream infections
- Sinusitis
- Clostridium difficile
- Intra-abdominal (cholecystitis, abscess, peritonitis)
- UTI, pyelonephritis
- Meningitis, encephalitis
- Cellulitis, necrotizing soft tissue infection, wound infection
- Septic arthritis, osteomyelitis
- Endocarditis
- Fungemia, fungal abscess

Investigations

- CBC, electrolytes, BUN/Cr, PT/INR, LFT
- Blood culture, urine culture, site specific culture
- ABG/lactate
- Procalcitonin
- Imaging studies: chest x-ray, site specific CT scan, US, etc.

Management

- Source identification and control as rapidly as possible
- Broad spectrum IV antibiotic therapy within first hour
- Early goal directed therapy within the first 6 hr
 - CVP 8–12 mm Hg, 12–15 mm Hg if mechanically ventilated
 - MAP \geq 65 mm Hg
 - UOP ≥ 0.5 ml/kg/hr
 - ScVO₂ \geq 70% or MVO₂ \geq 65%
- Fluid therapy to reach above CVP targets
- Administer vasopressors to maintain MAP \geq 65 mm Hg (norepinephrine with or without vasopressin as first choice)
- Inotropic therapy with dobutamine for sepsis induced cardiac dysfunction
- May consider corticosteroids when hypotension is not responding to fluid resuscitation and vasopressors (ACTH stimulation test is no longer recommended).
- Supportive therapy (ARDSnet ventilation strategy, glycemic control to keep blood glucose in the

140–160 mg/dl range, renal replacement, stress ulcer prophylaxis, DVT prophylaxis)

ARRHYTHMIAS

Bradyarrhythmia: HR < 60 bpm

Differential Diagnosis

- SA node dysfunction
 - Sinus arrest
 - SA conduction block
 - Sick sinus syndrome
- AV node dysfunction
 - First degree AV block
 - Second degree AV block Mobitz type I
 - Second degree AV block Mobitz type II
 - Third degree AV block
- Junctional escape rhythm
- Ventricular escape rhythm
- Sinus bradycardia

Management

- 12-lead EKG
- Atropine 0.5 mg IV bolus repeat 3–5 min (maximum 3 mg)
- Dopamine IV infusion 2–10 mcg/kg/min
- Epinephrine IV infusion 2–10 mcg/min
- Transcutaneous pacing (consider pacing for symptomatic bradycardias, 3rd degree AV block, Mobitz type II 2nd degree block)
- Transvenous pacing
- Treat underlying cause

Tachyarrhythmia: HR > 100 bpm

Differential Diagnosis

- Narrow complex tachycardia
 - Sinus tachycardia
 - Focal atrial tachycardia
 - Atrial fibrillation
 - Multifocal atrial tachycardia
 - Atrial flutter
 - Junctional tachycardia
 - AV node reentry tachycardia
 - AV reentry tachycardia
- Wide complex tachycardia
 - Monomorphic VT

- Polymorphic VT
- SVT with aberrancy
- Pre-excitement tachycardia (WPW)

Management

- 12-lead EKG
- If unstable (hypotension, altered mental status, signs of shock) then proceed to synchronized cardioversion
 - Narrow regular 50-100 J biphasic
 - Narrow irregular 120–200 J biphasic or 200 J monophasic
 - Wide regular: 100 J biphasic; if ineffective, increase J in a stepwise fashion
 - Wide irregular: Defibrillation dose (not synchronized)
- Vagal maneuvers for supraventricular tachycardia
- Adenosine 6 mg IV push (if regular) for paroxysmal supraventricular tachycardia
- β-blocker Metoprolol 2.5–5 mg IV
- Calcium channel blocker Diltiazem 0.25 mg/kg IV followed by infusion
- Amiodarone 150 mg IV over 10 min (may consider 150 mg iv repeated dose if unresponsive to first loading dose), followed by maintenance infusion (1 mg/min for 6 hr, reduced to 0.5 mg/min after that)
- Treat underlying cause

Atrial Fibrillation

Causes

- Alcohol intake
- Autonomic dysfunction
- Cardiac/thoracic surgery
- Cardiomyopathy
- Electrolyte abnormality
- Heart failure
- Hyperthyroidism
- MI
- Pericarditis
- Pulmonary disease
- Valvular heart disease

Management

- If unstable then synchronized cardioversion
 - 120-200 J biphasic
- If <48 hr consider cardioversion (DC or pharmacologic)
 - Pharmacologic cardioversion Amiodarone, Sotalol, Ibutilide, Flecainide
- If >48 hr rate control and anticoagulate (if no contraindications)
- Rate control
 - Metoprolol 5 mg IV q5min total of 15 mg
 - Diltiazem 0.25 mg/kg IV followed by infusion

- Digoxin 0.25 mg IV q2h total of 1.5 mg loading dose
- Amiodarone 150 mg IV over 10 min (may consider 150 mg iv repeated dose if unresponsive to first loading dose), followed by maintenance infusion (1 mg/min for 6 hr, reduced to 0.5 mg/min after that)
- Treat underlying cause

Hypotension

MAP < 60 mm Hg, SBP < 90 mm Hg, or decrease in SBP by >40 mm Hg from baseline. MAP = CO \times SVR

Differential Diagnosis

- Decrease in CO
 - · Decreased preload
 - Hypovolemia, hemorrhage, third spacing, decreased venous return, excessive PEEP
 - Decreased contractility
 - Myocardial infarction, myocarditis, cardiomyopathy, valvular failure, arrhythmia, congestive heart failure, drugs, electrolyte imbalance
 - Obstruction (to inflow or outflow of cardiac pump)
 - PE, tension pneumothorax, cardiac tamponade
- Decrease in SVR
 - Sepsis, SIRS, anaphylaxis, neurogenic shock, vasodilating drugs, adrenal insufficiency, liver failure due to decreased SVR

Management

- Hemodynamic monitoring (CVC, arterial line, PA catheter, echo)
- 500 ml NS or LR IVF bolus, then reassess hemodynamics (HR, BP, cardiac output [CO], index [CI], stroke volume, CVP) and repeat IVF bolus as needed
- Review medications, decrease dose of vasodilating drugs and cardiac depressants (sedatives, opiods, etc.)
- Vasopressors (norepinephrine, dopamine, phenylephrine, epinephrine)
- Inotropes (dobutamine, milrinone, levosimendan)
- Assess for and treat underlying cause

Нурохеміа

 $PaO_2 \le 60 \text{ mm Hg or } SpO_2 \le 90\%$

Differential Diagnosis

- Hypoventilation
 - COPD, asthma, bronchospasm, inappropriate ventilator settings
 - CNS depression drug overdose, CNS lesion
 - Obesity hypoventilation syndrome

- Neuromuscular weakness myasthenia gravis, critical illness polyneuropathy, Guillain–Barre syndromé, hypophosphatemia
- V/Q mismatch
 - Most common cause of hypoxemia in the ICU
 - Imbalance between lung perfusion and ventilation
 - Pneumonia, ALI/ARDS, pneumonitis, pulmonary edema, pulmonary embolism
- Right to left shunt
 - Intracardiac shunt, pulmonary AVM, hepatopulmonary syndrome
- Diffusion impairment (seen rarely in very advanced pulmonary fibrosis, asbestosis)
 - Usually occurs along with V/Q mismatch
 - Interstitial lung disease
- Reduced inspired FiO₂
 - High altitude, equipment failure

Investigations

- SpO₂
- ABG PaO₂, PaCO₂, A-a gradient
- PaO₂/FiO₂ ratio
- CXR, CT of chest if needed

Management

- Initially administer 100% FiO₂, titrate FiO₂ to SpO₂ > 90%
- Initiate mechanical ventilation if unresponsive to supplemental O2 therapy
- Appropriate ventilator settings (low tidal volume, higher PEEP, adequate RR)
- Ensure proper position of ET tube
- Bronchoscopy as needed (mucous plug, atelectasis, abundant secretions)
- Bag mask ventilation if considering equipment failure
- Treat underlying cause

PERICARDIAL TAMPONADE

Accumulation of pericardial fluid under pressure compressing all cardiac chambers resulting in cardiovascular collapse.

Differential Diagnosis

- Massive PE
- Acute MI with RV involvement
- Constrictive pericarditis
- Large pleural effusion
- Tension pneumothorax

Causes

• Inflammatory – RA, SLE

- Malignancy
- Uremia
- Hypothyroidism
- MI with free wall rupture
- Trauma
- Infectious viral, TB
- Cardiac interventions pacemaker placement, cardiac catheterization, heart surgery

Clinical Findings

- Tachycardia, pericardial friction rub
- Beck's triad Hypotension, JVD, muffled heart sounds
- Pulsus paradoxus
- Low voltage QRS, Electrical alternans
- Equilibration of diastolic pressures in all chambers of the heart CVP = RVEDP = PCWP = LVEDP

Management

- Diagnosis made with echocardiography
- Optimize preload with IVF bolus in hypovolemic patients
- Consider dobutamine, though heart is usually at maximum inotropic state via endogenous stimulation
- Definitive therapy is drainage via pericardiocentesis
- Cases of intrapericardial bleeding (trauma, post-op, tumor) usually require surgical intervention

TENSION PNEUMOTHORAX

Progressive accumulation of air in the pleural space that compresses the mediastinum kinking off venous return leading to cardiovascular collapse.

Differential Diagnosis

- Pericardial tamponade
- Hemothorax

Causes

- Thoracic trauma
- Iatrogenic CVC placement, transthoracic needle biopsies
- Spontaneous pneumothorax
- Secondary pneumothorax
- Barotrauma from mechanical ventilation

Clinical Findings

- Distended neck veins
- Progressive hypotension (often rapidly severe, may lead to cardiovascular collapse)
- Tracheal deviation to contralateral side
- Absent breath sounds

Management

- Immediate needle decompression with 14–16 gauge needle in the midclavicular line of the second intercostal space of affected side
- Followed by chest tube placement for definitive therapy

ACUTE MENTAL STATUS CHANGE

A spectrum of states including confusion, delirium, obtundation, stupor and coma.

Differential Diagnosis

- Stroke/hemorrhage
- Seizure
- Encephalitis/meningitis
- Delirium
- Post cardiac arrest brain injury/anoxic encephalopathy
- Drugs (illicit or medication overdose)
- Alcohol withdrawal
- Thiamine deficiency
- Hypo/hyperthyroid
- Adrenal insufficiency
- Hepatic encephalopathy
- Hypo/hyperglycemia
- Hypoxia/hypercarbia
- Electrolyte abnormality (hypo/hypernatremia, hypercalcemia, hypophosphatemia)
- Septic encephalopathy

Investigations

- Vitals signs
- CT head
- Labs electrolytes, BUN, Cr, CBC, LFTs, ammonia, UA, ABG
- Lumbar puncture to evaluate for meningitis/encephalitis
- EEG to evaluate for nonconvulsive status epilepticus

Management

- Establish and maintain ABCs (airway, breathing, circulation)
- Thiamine 100 mg IV (prior to dextrose to prevent precipitating acute Wernicke's encephalopathy)
- Dextrose 50 ml of D50W (25 g IV push)
- Naloxone 0.2–0.4 mg by slow (fractioned) IV push if comatose and suspect opiod intoxication
- Search for and treat underlying cause
- Flumazenil 0.2 mg iv maybe repeated 3 more times with a few minute intervals (to reverse the effects of benzodiazepines; beware of the potential seizures after reversal of benzodiazepine effect). Do not use in patients that chronically use benzodiazepines: the potential for intractable seizures is much higher in this group.

LOW URINE OUTPUT – ACUTE RENAL FAILURE

Oliguria with <400 ml/24 hr.

Differential Diagnosis

- Prerenal
 - Hypovolemia GI loss, hemorrhage, burns, sepsis, third spacing
 - Cardiac dysfunction MI, CHF, cardiomyopathies, arrhythmias
 - Vasodilatory shock sepsis, liver failure, anaphylaxis
- Renal
 - Ischemia/ATN trauma, surgery, sepsis, rhabdomyolysis
 - Nephrotoxic radiocontrast, antibiotics (aminoglycosides), NSAIDs
 - Vascular Wegener's, HSP, PAN
 - Glomerular glomerulonephritis
 - Interstitial AIN
- Postrenal
 - Malignancy, enlarged prostate
 - Nephrolithiasis
 - Obstructed urinary catheter
 - Papillary necrosis

Investigations

- Urine electrolytes
- Urinary sediment
- Urine osm
- Renal ultrasound
- Cardiovascular evaluation to r/o pump failure or hypovolemia
- Measure serum CK and myoglobin to r/o rhabdomyolysis

Management

- Flush or change foley
- IV fluid bolus to optimize intravascular volume status and hemodynamics
- Maintain MAP > 65 mm Hg to ensure renal perfusion
- If adequately volume loaded can consider diuretic (furosemide)
- Renal replacement therapy in cases of acidosis, electrolyte abnormality, volume overload, uremia
- Eliminate any nephrotoxins

FEVER IN THE ICU

Temperature >38.3°C (101.0°F)

Differential Diagnosis

- Infectious
 - Pneumonia

- Catheter-related blood stream infections
- Sinusitis
- C. difficile
- Intra-abdominal (cholecystitis, abscess, peritonitis)
- UTI, pyelonephritis
- Meningitis, encephalitis
- Cellulitis, necrotizing soft tissue infection, wound infection
- Septic arthritis, osteomyelitis
- Endocarditis
- Fungal
- Non-infectious
 - Neuro seizure, CVA/intracerebral hemorrhage
 - Pulmonary PE, ARDS, atelectasis, pneumonitis
 - Cardio pericarditis
 - GI pancreatitis, acalculous cholecystitis, mesenteric ischemia
 - Endocrine adrenal insufficiency, thyrotoxicosis
 - Inflammatory conditions SLE, vasculitis, polymyalgia rheumatica
 - Miscellaneous alcohol withdrawal/ delirium tremens, drug fever, neuroleptic malignant syndrome (NMS), malignant hyperthermia (MH), postoperative fever

Management

- Thorough history and physical exam looking for infectious etiology
- Obtain appropriate cultures (two sets of blood cx, urine cx, sputum cx) and imaging studies (CXR, Abd CT, etc)
- Source control (incise, drain, remove) of infection
- If signs of severe sepsis then broad spectrum antibiotics after obtaining cultures
- Consider non-infectious causes when infection site unclear from diagnostic tests
- If febrile >48 hr:
 - Remove central lines
 - If diarrhea present evaluate for *C. difficile*
 - Consider antifungal therapy
 - Ultrasound to evaluate for acalculous cholecystitis
 - IV dantrolene (2.5 mg/kg, more if needed) is the specific acute phase therapy for Malignant Hyperthermia related to anesthesia

MONITORING

SAMUEL M. GALVAGNO, JR., DO, PhD • ANQUENETTA L. DOUGLAS, MD

Noninvasive Monitoring

Electrocardiogram (ECG) – see www.ecglibrary.com for sample images

- Can detect transmural and subendocardial ischemia when leads are properly positioned
- Lead V₅ has been validated and found to detect 75% of ischemic changes seen in other leads
- The combination of leads II, V_2 , V_3 , V_4 , and V_5 has been shown to be over 90% sensitive for detecting ischemia

Temperature Monitoring

- Core temperature is best estimated from the nasopharynx, bladder, esophagus, or rectum
- Rectal temperature lags behind pulmonary artery and tympanic temperature in cardiac surgical patients during the rewarming period after bypass
 - The same is true for patients in shock
 - This is due to decreased splanchnic blood flow
- Subjective assessment of skin temperature may be misleading in some instances (Heart Lung. 2010;39:27)

Pulse Oximetry (SpO₂)

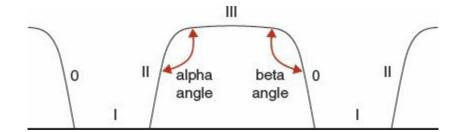
- Monitors oxygen saturation; monitors oxygenation, not ventilation
- Has the potential to increase vigilance and detect hypoxemia
- Based on the Beer-Lambert law
 - The concentration of a substance can be determined by transmitting a known intensity of light through a solution
 - Red light (660 nm) and near-infrared light (940 nm) are transmitted through a vascular bed (typically a finger)
 - Both of these types of light readily penetrate tissue whereas other wavelengths of light are absorbed
 - 660 nm light is absorbed by reduced hemoglobin
 - 940 nm near-infrared light is absorbed preferentially by oxygenated hemoglobin
 - A photodiode detector measures the amount of light transmitted, and the red/near-infrared ratio is calculated and compared with reference values
- The pulse-added component discriminates from venous blood or connective tissue from arterial blood
- Limitations:
 - Nail polish and dark skin may cause variable interference
 - Hypovolemia, vasoconstriction, or peripheral vascular disease may cause a low signal-to-noise ratio and inaccurate measurements
 - Extra ambient light and excessive motion may cause artifacts
 - Dyshemoglobinemias are a well-established cause of optical interference

- Both carboxyhemoglobin and methemoglobin absorb light within the red and near-infrared wavelength ranges
 - A co-oximeter offers a multi-wavelength analysis that takes into account these absorptions
- With methemoglobinemia, standard oximeters falsely detect a greater degree of absorption of both hemoglobin and oxyhemoglobin, increasing the absorbance ratio
 - When the absorbance ratio reaches 1, the calibrated saturation level approaches a plateau of approximately 85%
 - The SpO₂ reading will remain at 85%
- With carboxyhemoglobin, red light is falsely absorbed, and the SpO₂ will be falsely high
- Despite prevalent usage, there is little evidence that pulse oximetry prevents deaths, complications, or readmissions to the ICU (Crit Care Med. 1988;16:701; Cochrane Database Syst Rev. 2009;Oct7;4:CD002013)
 - Nevertheless, monitoring oxygenation with pulse oximetry is a standard of care in the ICU

Capnography (see www.capnography.com for more information)

- Refers to the digital display of CO₂ on a digital or analog monitor
- Is a standard monitor for non-invasively measuring ventilation
- Indications in the ICU
 - Confirmation of endotracheal intubation
 - Noninvasive monitoring of ventilation (especially during positional changes)
 - Assessment of cardiac output (see additional section below)
 - Prognosis when CPR is required
 - Prediction of outcome during resuscitation for trauma
 - Confirmation of needle placement during percutaneous dilatational tracheostomy
 - Colorimetric CO₂ detection *or* capnography has become the standard of care for confirming that an endotracheal tube has been placed correctly (in addition to other clinical determinants)
 - A purple color corresponds to an ETCO₂ level <0.5%, a tan color indicates ETCO₂ of 0.5%–2%, and a yellow color indicates end-tidal CO₂ (ETCO₂) >2%
 - Normal end-tidal CO_2 is >4%; hence, the device should turn *yellow* when the endotracheal tube is inserted in patients with intact circulation
- Infra-red (IR) spectrography is the most commonly used method for measuring ETCO₂
 - IR rays are absorbed by polyatomic gases such as nitrous oxide, CO2, and water vapor
 - CO₂ selectively absorbs specific wavelengths (4.3 μm) of IR light
 - The CO₂ concentration measured by the monitor is usually expressed as partial pressure in millimeters of mercury
 - Some units display % CO₂
- Current terminology for capnograms is depicted in this Figure 1.

Figure 1. The Phases of a Capnogram. Phase II Indicates the Beginning of Expiration; Phase 0 Indicates Inspiration. See *www.capnography.com* for details



- Under normal circumstances, ETCO₂ is lower than PaCO₂ by 2–5 mm Hg
 - This gradient is caused by ventilation/perfusion mismatching in the lungs
 - This gradient may change in hemodynamically unstable patients or when there are abrupt changes in cardiac output
- The ETCO₂/PaCO₂ fraction is a measure of alveolar dead space
 - Provides an indirect measure of ventilation/perfusion mismatching in the lung
- Reductions in ETCO₂ also occur with decreased cardiac output and pulmonary blood flow
- Causes of increased or decreased ETCO₂ are reviewed in the Table below.

Causes of Increased or Decreased ETCO ₂				
Increased ETCO ₂	Decreased ETCO ₂			
Hypoventilation	Hyperventilation			
Hyperthyroidism/thyroid storm	Hypothermia			
Malignant hyperthermia	Venous air embolism			
Fever/sepsis	Pulmonary embolism			
Rebreathing	Decreased cardiac output			
Other hypermetabolic states	Hypoperfusion			

Noninvasive Blood Pressure Measurement

- Measured by an electronic pressure transducer that detects oscillating blood flow as the cuff is slowly deflated
- If the upper extremity used, the brachial artery is compressed and oscillates as restricted blood flows during systole and diastole
- The mean arterial pressure is generally the most accurate component of this type of noninvasive blood pressure measurement
- Some studies have shown that oscillatory measurements are often lower than invasive blood pressure measurements
- Use of improperly sized cuffs is a common source of error

Brain Monitoring

- Useful when heavy sedation is required with or without the use of muscle relaxants
 - Awareness under anesthesia is estimated to occur in 0.1%–0.2% of all patients undergoing general anesthesia; the risk may be higher for ICU patients who require prolonged sedation with or without muscle relaxation
 - Awareness during sedation or paralysis in the ICU has not been as thoroughly studied as in the general surgical population
- Several brain monitors based on electroencephalographic (EEG) indices are commercially available
 - The Bispectral Index (BIS; Aspect Medical Systems, Norwood, MA) is the best studied and the most widely used brain monitor

- A dimensionless index is calculated using a proprietary algorithm derived empirically by recording EEG data from healthy adults undergoing various levels of anesthesia
 - The index ranges from 0 to 100
 - BIS values between 45 and 60 are considered ideal for surgical anesthesia
 - BIS levels <45 have been associated with poor outcomes, including increased morbidity and mortality
- Other brain monitors include the Entropy Index, the Cerebral State Index, and the SEDLine monitor (Maisimo Corp, Irving, CA)

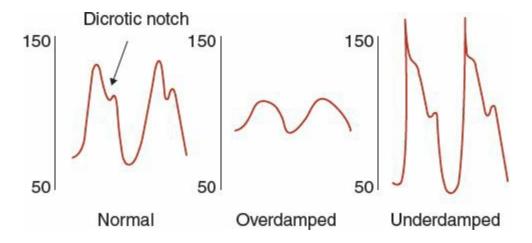
Invasive Monitoring

Direct Arterial Pressure Monitoring

- Indications:
 - Continuous blood pressure measurement, need for beat-to-beat BP monitoring
 - Need for frequent arterial blood gas determinations or blood sampling
 - When noninvasive blood pressure monitoring is not reliable or possible
- Common locations for cannulation include the radial, femoral, dorsalis pedis, brachial, and axillary arteries
 - The radial artery is the most commonly utilized site
 - The ulnar artery has been reported in some studies to be larger, but is typically avoided due to proximity to the ulnar nerve and the potential for hand ischemia
 - Although most texts report the ulnar artery to be larger than the radial artery, significant anatomical variation exists (Anesth Analg. 2009;109:1763)
 - The few studies addressing the use of the ulnar artery for cannulation have reported a safety and efficacy profile comparable to radial artery cannulation
- Contraindications:
 - Infection at the cannulation site
 - Lack of collateral flow
 - Can be assessed with the Modified Allen's test for radial cannulation:
 - Pressure is held firmly over the radial and ulnar arteries
 - The patient clenches his or her fist several times until the palmar skin is blanched
 - The patient unclenches the fist, and the ulnar artery pressure is released while maintaining pressure on the radial artery
 - The time for palmar capillary refill is noted; brisk return of skin color indicates adequate collateral circulation as supplied by the ulnar artery
 - The test is not reliable for predicting hand ischemia after radial artery cannulation
 - Other assessments include addition of a pulse oximeter during the Allen's test, Doppler ultrasound, and plethysmography
 - Lymphatic disruption at the site of insertion
 - Arterial insufficiency at the site of insertion
- Complication rates (radial artery):
 - Hematoma − 14.4%
 - Catheter-related bacterial colonization 1%–22%
 - Local infection 0.72%

- Bleeding -0.5%
- Sepsis -0.13%
- Pseudoaneurysm 0.09%
- Permanent hand ischemia 0.09%
- Catheter maintenance after placement
 - Current guidelines from the Centers for Disease Control do not recommend routine replacement of peripheral arterial catheters at fixed intervals to prevent infections
 - Many institutions now suggest that maximum barrier precautions (as used during placement of central venous lines) should be used for arterial lines since some studies have shown similar infection rates (Crit Care Med. 2010;38(4):1030)
 - Heparinized solutions are considered to be advantageous by some regarding maintaining catheter patency
 - Complications from this practice include antibody formation causing heparin-induced thrombocytopenia and altered anticoagulation tests
- Interpretation
 - The dicrotic notch (see Figure 2) indicates closure of the aortic valve, indicating the end of systole or the ejection phase of the heart
 - Systolic pressure increases as the arterial pressure waveform moves away from the aorta toward the peripheral arteries
 - The systolic pressure may be up to 20 mm Hg greater in the radial or femoral arteries than at the aortic root
 - The mean arterial pressure remains the same, regardless of the distance of the catheter from the aorta
 - The transducer should be leveled at the phlebostatic axis
 - This corresponds to the right atrium, and may be estimated by locating the fourth intercostal space at the halfway point between the anterior–posterior diameter of the chest
 - After zeroing, the pressure will be artificially elevated or decreased if the transducer is moved
 - This is because for every 1 cm movement, pressure may change by 0.7 mm Hg
 - For example, if the arm is elevated 1 cm above the phlebostatic axis, the pressure will be artificially lower by approximately 0.7 mm Hg
 - For every cm the arm is lowered below the phlebostatic axis after zeroing, the blood pressure will be artificially elevated by 0.7 mm Hg per cm

Figure 2. Examples of Normal, Overdamped, and Underdamped Arterial Waveforms



- Troubleshooting
 - Waveforms may be overdamped or underdamped (see Figure 2)
 - Overdamping is usually the result of air bubbles and can be fixed by flushing the system
 - Underdamping is usually the result of lengthy connector tubing
 - A flush test can also be used to determine if the system is underdamped or overdamped
 - If the flush test does not produce any oscillations, the system is likely overdamped
 - If the flush test produces many post-flush oscillations, system is likely under-damped

Central Venous Pressure (CVP)

- Indications:
 - Measurement of CVP
 - Surrogate marker for cardiac preload
 - Measurement of central mixed-venous oxygen (ScVO₂)
 - Use for pulse wave analysis/minimally invasive cardiac output determination (e.g., PiCCO system)
- Interpretation of CVP waveforms (see Figure 3)
 - a wave: corresponds to P wave on ECG; indicates atrial contraction
 - *c wave:* corresponds to QRS on ECG; indicates elevation of the tricuspid valve into the right atrium during early ventricular contraction
 - *x descent*: occurs before the T wave; caused by downward movement of the ventricle during systolic contraction
 - *v wave:* corresponds to T wave; reflects the pressure produced when the blood filling the right atrium comes up against a closed tricuspid valve
 - y descent: occurs when the tricuspid valve opens

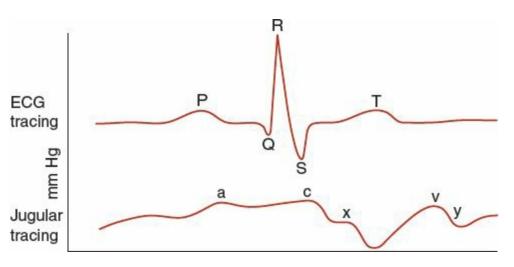


Figure 3. CVP Waveforms

- CVP waveform anomalies
 - Absence of a waves: atrial fibrillation
 - "Cannon a waves:" atrioventricular dissociation (i.e., heart block or junctional rhythm)
 - Tricuspid regurgitation: c wave and x descent is replaced by a large positive wave of regurgitation as blood flows back into the right atrium during ventricular contraction
 - Cardiac tamponade: all pressures are elevated; absent y descent
- Problems with CVP interpretation and use in the ICU

- CVP does not accurate predict fluid responsiveness since there is a very poor correlation with CVP and blood volume (Chest. 2008;134:172)
- Impaired right ventricular function, severe pulmonary disease, or valvular heart disease affect the CVP reading
- CVP does not correlate well with stroke volume (Curr Heart Fail Rep. 2010;7:116)
- Complications
 - Pneumothorax
 - Infection
 - Hemorrhage
 - Thrombus/embolism
 - Dysrhythmias

Pulmonary Artery Catheter

- Despite controversy regarding its use, remains the gold standard for cardiac output determination (Figure 4).
 - Remains a valuable tool when used in selected patients

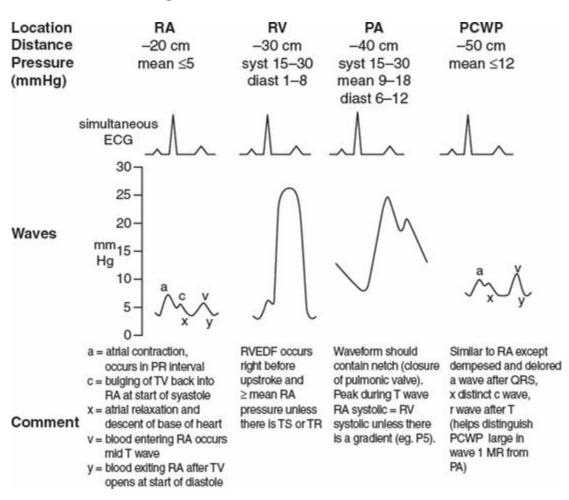


Figure 4. PA Catheter Waveforms

PCWP waveform abnormalities large a wave \rightarrow ! micral stenosis; large v wave \rightarrow ! mitral regurgitation; blanted y descent \rightarrow ! tamponade; steep x & y descents \rightarrow ? constriction from Pocket Medicine by Sabatine, 4th Ed, 2011.

- Provides information on 3 key variables: (1) intrathoracic intravascular pressures, (2) cardiac output, and (3) mixed venous oxygen saturation (SvO₂)
- Thermodilution technique

- The thermal indicator, typically 10 ml of room temperature saline, is injected into the central venous circulation
 - The resulting temperature change is detected in the pulmonary artery
- Cardiac output is calculated from the area under the thermodilution curve with the modified Stewart-Hamilton equation
 - When the area under the curve is *increased*, the cardiac output is low
 - When the area under the curve is *decreased*, the cardiac output is high
 - Conditions that affect cardiac output:

Conditions That May Effect Thermodilution-Derived Measurements of Cardiac Output					
Overestimate	Underestimate	No Change	Impossible to Predict		
Left → right or right → left intracardiac shunts Use of <10 ml of injectate Infusion of warm blood or fluids through a side port Encapsulation of the thermistor around a clot	Use of >10 ml of injectate Use of colder than room temperature injectate Presence of infusions running simultaneously through an infusion port on the catheter	Mitral regurgitation Tricuspid regurgitation Cold ambient temperature	Looping of the catheter Choice of an incorrect constant ('K' in the Stewart-Hamilton equation) for the particular catheter		

Indications

- Differentiation of types of shock
- Assessment of pulmonary edema (ARDS vs. cardiogenic)
- Diagnosis and monitoring of pulmonary hypertension
- Diagnosis of valvular disease, intracardiac shunts, cardiac tamponade, pulmonary embolism
- Assessment of hemodynamic response to therapies
 - Especially in instances when other conventional therapeutic endpoints are not feasible or reliable (e.g., lack of urinary output in a patient with renal failure)
- Monitoring and management for patients with heart failure or significant cardiac dysfunction
- Contraindications
 - Coagulopathy
 - Prosthetic right heart valves
 - Endocardial pacemaker/defibrillator (relative contraindication)
 - Left bundle branch block (may precipitate complete heart block)
 - Right-sided endocarditis
 - Poorly controlled dysrhythmias
 - Right ventricular thrombus
- Technique for insertion (see typical PA pressures and waveforms in Figure 4)
 - The catheter is inserted into the introducer port of a large bore single lumen central line (typically an 8, 8.5, 9, or 10 French cordis introducer) placed in the subclavian or internal jugular vein
 - The catheter is advanced past the length of the introducer port
 - Pressure is monitored continuously during insertion
 - The balloon is inflated with no more than 1.5 ml of air once in the superior vena cava

- The catheter is advanced with the balloon inflated, and the position in the heart is determined by the pressure tracings
- The pulmonary artery occlusion pressure (PAOP) is a venous-type pressure waveform with the same value as the pulmonary diastolic pressure (Figure 4)
 - This pressure reflects a static column of pressure from the left atrium, and reflects leftventricular end diastolic pressure
 - A normal PAOP is 6–12 mm Hg
 - The pulmonary capillary wedge pressure (PCWP) if often regarded as a synonym for the PAOP
 - Technically, the PCWP is reached when the catheter is "wedged" as distally as possible in the pulmonary artery as opposed to the PAOP which is the first pressure measured when the artery is occluded
- Once the PAOP appears the balloon is deflated, and the catheter is either locked in place or withdrawn slightly
 - Pulmonary artery waveforms should appear again (PA in previous figure)
- Some pearls and pitfalls for successful placement and interpretation
 - When inserted from the right jugular vein, the right atrium should be encountered within 20 cm from skin entry of the catheter
 - From the right atrium, the right ventricle should be encountered within 20 cm
 - From the right ventricle, the pulmonary artery should be encountered within 20 cm (typically <60 cm from the site of skin insertion)
 - The PAOP should be measured at end-expiration
 - At this point in the breathing cycle, average transmural pressure is best estimated
 - Correct measurement is imperative (Crit Care Med. 2008;36(11):3093)
 - Zeroing, calibration, and elimination of artifacts is mandatory
 - Many errors are made in data collection when these tasks are not accomplished
 - Newer catheters can provide continuous measurements of parameters
- Complications
 - Pneumothorax (during placement of introducer line; 1%–2%)
 - Right bundle branch block (0.1%–5%)
 - Dysrhythmias (often self-limiting)
 - Pulmonary artery rupture (0.2%)
 - Central line associated bloodstream infection
 - Thrombosis
 - Endocarditis
 - Knotting of catheter
- Interpretation
 - The reader is referred to an outstanding free educational reference for pulmonary artery catheter waveform and data interpretation at http://www.pacep.org

Interpretation of Pulmonary Art	ery Catheter Find	ings	
Condition/Type of Shock	PAOP/PADP	CO/CI	SVR
Distributive shock (sepsis, anaphylaxis, neurogenic)	Normal/1	1	1
Cardiogenic	1	1	1
Hypovolemic	1	1	1
Obstructive (tension pneumothorax)	1	1	1
Pulmonary embolism	Normal/1	1	1
Pericardial tamponade*	= Central venous pressure	1	1

^{*}Classic finding: near-equalization of right atrial, central venous, and pulmonary artery diastolic pressures. PADP, pulmonary artery diastolic pressure; CO, cardiac output; CI, cardiac index; SVR, systemic vascular index.

MINIMALLY INVASIVE HEMODYNAMIC MONITORING

- Carbon dioxide rebreathing: measurement of cardiac output based on the Fick principle of cardiac output estimation (NiCCO; Respironics, Murraysville, PA)
 - Postulates that blood flow through alveoli is equal to the uptake or elimination of a gas divided by the difference in concentrations of that gas in the blood flowing in and out of the lungs
 - Compares ETCO₂ obtained during a non-rebreathing period with that obtained during a subsequent rebreathing period
 - Measures nonshunted portion of cardiac output
 - Estimates Qs/Qt using a shunt correction algorithm
 - SpO₂ from a pulse oximeter and FiO₂ must be measured
 - Validation studies have yielded inconsistent results
 - Has not demonstrated superiority to thermodilution cardiac output techniques
- Pulse wave analysis (LiDCO; LiDCO Ltd, Cambridge, UK)
 - Transpulmonary indicator dilution is performed using small doses of lithium (<1% of levels used pharmacologically)
 - Serves to calibrate the system
 - Based on principle of mass/power conservation
 - A linear relationship between net power and net flow is assumed in the vascular system
 - Pulse wave is analyzed by a complex mathematical function
 - Requires only an arterial line; a central line is not required
 - Reliably estimates continuous cardiac output in hemodynamically stable patients
 - Calculates stroke volume variation (SVV) and pulse pressure variation (PPV)
 - Principle indication is stroke volume optimization in the perioperative setting
 - Results may be altered by high doses of muscle relaxants, electrolyte disorders, vasoactive medications, and changes in hematocrit
 - Cannot be used in patients taking lithium

• Esophageal Doppler

- Cardiac output is calculated based on the diameter of the aorta, the distribution of cardiac output to the descending aorta, and the measured blood flow velocity in the aorta
- Limitations
 - Assumes constant aortic cross-sectional area; this is often dynamic and varies amongst patients
 - Accurate measurements are highly dependent on correct positioning of the probe; 10–12 probe

insertions are recommended to attain competency (Intensive Care Med. 1998;24:347)

- Cannot reliably produce continuous cardiac output measurements
- Has demonstrated modest correlation with pulmonary artery catheter thermodilution techniques

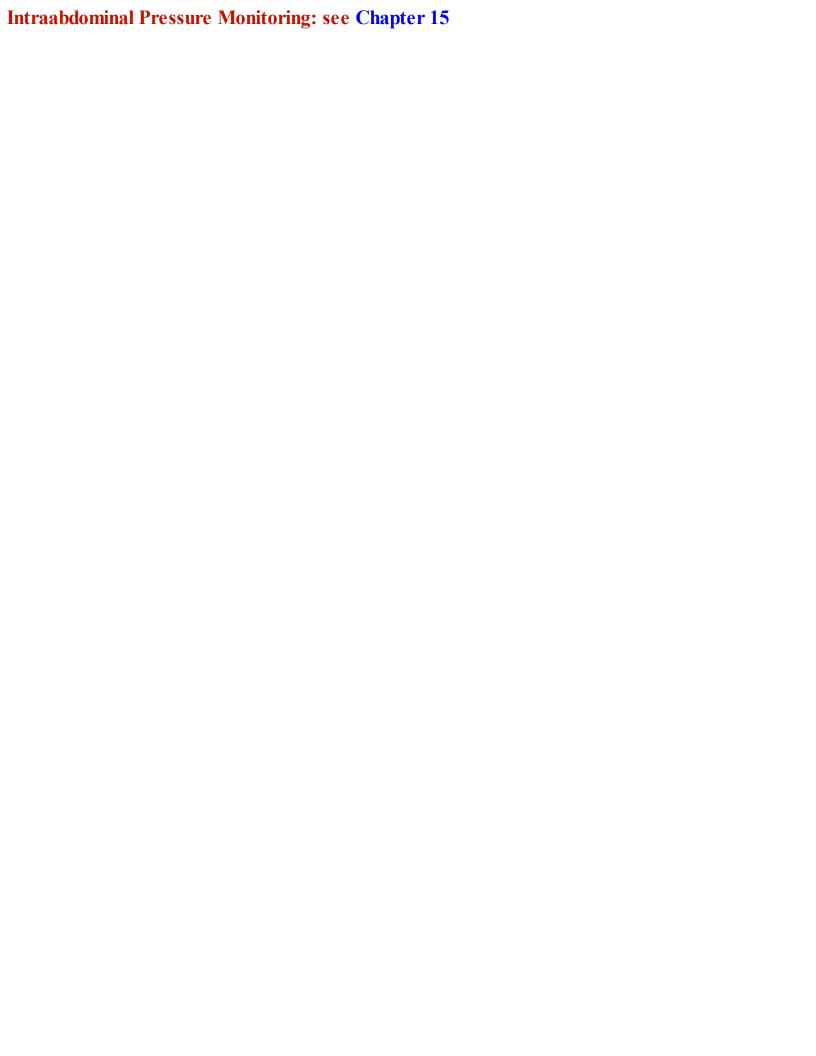
• Plethysmography/thoracic electrical bioimpedance

- Electrical resistance (impedance) across the chest is measured
 - The lower the fluid content, the higher the resistance (fluid conducts electricity)
 - With newer devices, correlation between this technique and traditional thermodilution techniques with a pulmonary artery catheter is improving

• Echocardiography (see also Chapter 41)

- Applications of bedside transthoracic echocardiography in the ICU
 - Diagnosis of cardiac tamponade
 - Cardiac output measurement
 - Assessment of left ventricular function
 - Assessment of right cardiac function and leftward septal shift
 - Intracavitary pressure measurements
 - Assessment of fluid responsiveness
- Transesophageal echocardiography (TEE) is a minimally invasive technique that provides a rapid, real-time assessment of cardiac anatomy and functional status
- Bedside lung ultrasound may be used to evaluate pleural effusion, pneumothorax, ARDS, pulmonary edema, or lung consolidation (Minerva Anesthesiol. 2009;75:509)
- Arterial Pressure Waveform Analysis Not Requiring External Calibration (FloTrac/Vigileo; Edwards Lifesciences, Irvine, CA)
 - Analyzes arterial pressure waveform in conjunction with patient demographic data to calculate cardiac output
 - Patient weight, height, and age are entered
 - Algorithm is based on the principle that the pulse pressure is proportional to stroke volume and inversely proportional to aortic compliance
 - Requires placement of an arterial catheter pressure sensor
 - Provides continuous cardiac output
 - Acceptable agreement has been found when compared with conventional thermodilution techniques (pulmonary artery catheter)
 - Patients on vasopressors may not have reliable measurements
- Systolic Pulse Contour Analysis with Transpulmonary Thermodilution Calibration (PiCCO; Pulsion Medical Systems, Munich, Germany)
 - Uses a dedicated thermistor-tipped catheter which is usually placed in the femoral artery
 - Tracks changes in stroke volume on a beat-to-beat basis
 - Radial or brachial thermistor-tipped catheters may be used as well
 - A central venous line is required to perform cardiac output determination with transpulmonary thermodilution
 - Device calibration is required every 8 hr in hemodynamically stable patients
 - Calibration needs to be done more frequently in unstable patients
 - Several studies have validated the PiCCO system by comparing it with conventional thermodilution techniques (pulmonary artery catheter)
 - In addition to cardiac output, estimates static preload variables such as global end-diastolic volume (GEDV) and extra-vascular lung water (EVLW)

Calculates functional variables such as PPV and SVV	



MECHANICAL VENTILATION AND PULMONARY ISSUES

REBECCA M. BARON, MD

VENTILATION, PULMONARY PHYSIOLOGY, VENTILATOR MANAGEMENT

Gas Exchange

Oxygenation:

1. Is there an A-a (Alveolar-arterial O_2) gradient?

• Alveolar gas equation (most accurately determined on room air or 100% F_IO₂ on ventilator; PAO₂ is alveolar partial pressure of O₂; PaO₂ is arterial partial pressure of O₂; P_{ATM} is atmospheric pressure; PH₂O is saturated vapor pressure of water; PaCO₂ is partial pressure of CO₂, F_IO₂ is fraction of inspired gas that is O₂):

$$PAO_2 = (F_1O_2 \times (P_{ATM} - PH_2O)) - \frac{PaCO_2}{RQ}$$

• Where $P_{ATM} = 760 \text{ mm Hg}$, $PH_2O = 47 \text{ mm Hg}$, RQ (respiratory quotient) = 0.8, then:

$$PAO_2 = (F_1O_2 \times 713) - \frac{PaCO_2}{0.8}$$

• On room air (FIO2 = 0.21):

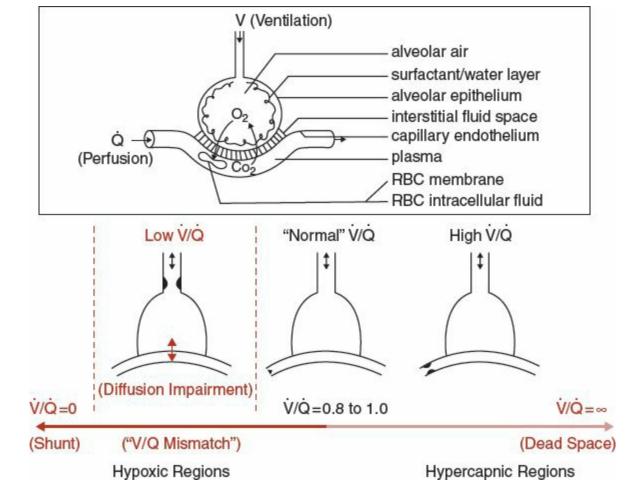
$$PAO_2 = 150 - \frac{PaCO_2}{0.8}$$

A-a gradient: PAO₂ - PaO₂

• Normal gradient:
$$4 + \frac{\text{age}}{4}$$
 (e.g., about 9 for a 20-yr old)

- If an A-a gradient is NOT present, then *alveolar hypoventilation* must be considered as a mechanism of hypoxemia.
- 2. If there is an A-a gradient, is the hypoxemia responsive to $100\% F_1O_2$?
- If there is an A-a gradient, then V/Q mismatch, shunt, or diffusion impairment must be considered (though diffusion impairment is rare unless very severe lung disease is present); if the hypoxemia is NOT responsive to 100% F_IO_2 , then is consistent with shunt; if is responsive to 100% F_IO_2 , then likely is V/Q mismatch see Figure 1.

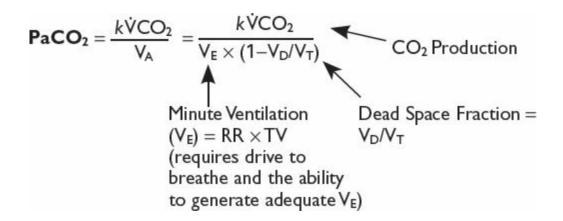
Figure 1. Overview of Ventilation–Perfusion Relationships



- V/Q mismatch: regions of low V/Q, usually caused by alveolar filling (blood, pus, or water), and hypoxemia usually O_2 -responsive
- Shunt: regions where V/Q = 0, can be intrapulmonary, e.g., from atelectasis, or extrapulmonary; not O_2 -responsive in that PaO_2 doesn't significantly increase or at least rise above 100 mm Hg with 100% F_1O_2 administration
- Diffusion impairment: rare cause of hypoxemia but possible with severe barrier to gas exchange from interstitial lung disease or pulmonary hypertension

Ventilation:

Determinants of PaCO2



k, constant; V_A , alveolar ventilation; V_E , minute ventilation; RR, respiratory rate; TV and V_T , tidal volume; V_D , dead space.

• Thus, PaCO₂ determined by balance of CO₂ production (e.g., increased work of breathing [see

below], increased metabolism, fever, etc.) and elimination of CO_2 (ability to generate adequate minute ventilation). Efficiency of CO_2 elimination determined in part by physiologic dead space (e.g., proportion of alveoli ventilated but not perfused) and can be measured using endtidal CO_2 device hooked up to exhalation port of ventilator that measures P_ECO_2 (exhaled CO_2), where V_D/V_T is dead space fraction and $PaCO_2$ is arterial CO_2 :

$$V_D/V_T = \frac{PaCO_2 - P_ECO_2}{PaCO_2}$$

- Fatigue: Imbalance of supplies (O₂, nutrition, energy extraction) and demand (work of breathing, muscular strength, and efficiency)
 - Work of breathing: proportional to mean pressure per breath required of inspiratory muscles (P_I) and minute ventilation; increased with elastic (e.g., edema) or resistive load (e.g., asthma)
 - Efficiency: ratio of external work performed to energy consumed; e.g., poor efficiency in emphysema perhaps due to flattened diaphragm and disadvantageous force/length relationship

General:

- Indications for intubation (and parameters to consider when weaning)
 - Refractory hypoxemia
 - Ventilation impairment (and failed or non-candidate for non-invasive ventilation)
 - Mental Status/Airway protection
 - Secretion management (often in conjunction with issues above)
 - "Other": e.g., Metabolic acidosis, airway protection for procedure, etc.
- Initial settings:
 - Choose a "standard" mode you're comfortable with
 - All modes require understanding and monitoring of same principles
 - Generally, AC mode safest with full support, though patients will usually need sedation and 'acclimation' to be in synchrony
 - Unless specific reason, try to set tidal volumes in 6–8 cc/kg (see Chapter 5 on ARDS management) with RR generally 10–12 and guided by pH/minute ventilation
 - Initial F_IO₂ settings usually 100%, but try to wean down as quickly as possible, as long as maintaining adequate oxygenation
 - Often will choose "physiologic" PEEP (positive end-expiratory pressure) of 5 cm H₂O, unless other factors (see Chapter 5 on ARDS)
 - Flow rates on standard volume-cycle modes usually set at 60 l/min (1 l/sec) but can adjust (see COPD below); correlative setting on PCV is setting inspiratory time (I-time); in aggregate, flow and I-time settings determine inspiratory:expiratory (I:E) ratios.

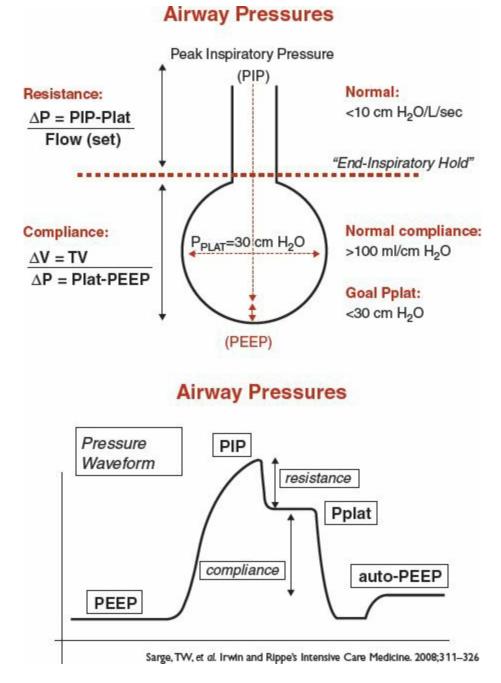
	Modes of Mech	anical Ventilation	
Ventilator mode (of note, names of modes based upon Puntan-Bennett venti- lator — other ventilators have similar modes with different names)	Parameter(s) Set ("Controlled" Parameters)	Parameter(s) Monitored ("Variable" parameters)	Comments
"Standard Modes"			
Assist-control (AC)	Tidal volume (TV), Respiratory rate (RR), Flow	Peak and plateau pressures	Every breath taken by patient (including spon- taneous) are delivered at set TV
Synchronized intermittent mandatory ventilation (SIMV)	TV, RR, Flow	Peak and plateau pressures	Spontaneous breaths aren't supported
Pressure control ventilation (PCV)	Driving pressure, inspiratory time, RR	TV (flow can be variable within set parameters)	PCV can be set in"AC" mode (each breath sup- ported by set driving pressure) or "SIMV" mode
Pressure support ventilation (PSV)	Or hing pressure (also set % rise which determines how fast the pre-set pressure is delivered and E _{tors} , often at 25% of peak flow, which determines onset of exhalation)	TV, RR, flow	No back-up raits (except apnea mode from ventilator), so patient must be able to main- tain adequate minute ventilation
"Newer Modes" Use with experienced personnel available to assist and guide			
Volume Control Plus (VC+) (termed Pressure Regulated Volume Control [PRVC], on Servo ventilator)	Targeted TV, Inspiratory time, RR	TV, RR, Pressure delivered and flows variable; Monitor peak pressures; Estimated driving pressure needed to deliver targeted TV: PIP – PEEP	Volume-targeted pressure ventilation in PCV mode: Set targeted TV, and machine makes determination from 3 delivered breaths as to required pressure to deliver volume; thus, parameters of ventilation can change
Volume Support Plus (VS+)	Targeted TV, %Rise, E _{arm}	TV, RR, Reak pressures (as above for VC+)	As above, for VC+, except delivered breaths using PSV mode
Bilinei Ventilation	High and Low pressure levels (PEEP _{Np} and PEEP _{Erol}); cycling synchronized with patient breathing with time set at higher PEEP (T _{lop}); PSV set for spontaneous breaths; Airway Pressure Release Ventation (APRV) represents Blevel with very short periods of time released from PEEP _{Np} for long Tup settings)	Minute ventilation, peak pressures; driving pressure on spontaneous breaths is determined by PSV set pressure minus difference between PEEP _{hit} and PEEP _{hit} (e.g., if PSV is set at 20 cm H ₂ O, and PEEP _{hit} is 20 cm H ₂ O, PEEP _{hit} is 5 cm H ₂ O, then driving pressure is PSV — PEEP _{hit} — PEEP _{hit} or 5 cm H ₂ O!	May have higher risk of barotraums; not clearly beneficial above other modes; similar to PCV mode if patient not breathing spontaneously; oxygenation adjusted with PEEP _{the} and ventila- tion via PEEP _{thelies} gradient or via increased PSV on spontaneous breaths.

RR, respiratory rate; PEEP, positive end expiratory pressure; P, pressure; T, time.

Monitoring patients on the ventilator (measure on volume-cycled ventilation with square wave and constant flow [ideally 60 l/min or 1 l/sec to facilitate calculations]; measurements may be more accurate with patient sedated):

- Measurement of peak inspiratory pressure, plateau pressure (end-inspiratory hold to derive estimate of alveolar pressure); in patients heavily sedated or paralyzed, can perform an end-expiratory hold to measure intrinsic PEEP (auto-PEEP), which can indicate gas-trapping
- Calculation of resistance and compliance can assist in monitoring and managing ongoing issues on the ventilator (see Figure 2):
 - "High PIPs" or peak inspiratory pressures can arise from problems with elevated *resistance* (increased peak pressure relative to plateau pressure) and/or reduced *compliance* (increased plateau pressure for given TV)
 - Examples of conditions causing increased resistance (airflow obstruction):
 - Bronchoconstriction
 - Mucus plugging
 - Ventilator tubing or endotracheal tube obstruction

Figure 2. Description and Measurement of Airway Pressures in Patients on Mechanical Ventilators



P, pressure; PIP, peak inspiratory pressure; Plat, plateau pressure (in this example, Pplat is 30 cm H_2O); V, volume; TV, tidal volume; PEEP, positive end expiratory pressure.

- Examples of conditions causing reduced compliance (lung stiffness):
 - Tension pneumothorax
 - Congestive heart failure
 - Pulmonary hemorrhage
 - Pneumonia/ARDS

Acute Failure to Liberate from Ventilator Support

Causes

- Incomplete resolution of illness precipitating mechanical ventilation
- Development of new condition limiting independent ventilation
- Neurological-prolonged sedation, critical illness polyneuropathy, inadequate pain control
- Muscular-atrophy, critical illness myopathy, diaphragmatic paralysis
- Cardiovascular-decreased oxygen delivery, LV failure, RV dysfunction or failure

- Pulmonary–flail chest, non-compliant chest wall, pleural effusions, airway obstruction, intrinsic PEEP
- Abdomen—tight surgical dressings, tense ascites, intra-abdominal hypertension
- Nutrition—protein calorie malnutrition
- Electrolytes-hypophosphatemia, hypomagnesemia, hypokalemia, hypocalcemia
- Infectious Disease–VAP, underlying sepsis, resistant microorganisms

Investigations after careful physical examination might include:

- Labs-electrolytes, pre-albumin, CRP, ABG, blood, sputum, stool, urine cultures
- Radiographic imaging, echocardiogram
- Respiratory mechanics, check bladder pressure

Respiratory Failure and Ventilator Management (Eur Respir J Suppl. 2003;47:3s)

Respiratory failure can be "Lung"/Gas exchange/Hypoxemic vs. "Pump"/Ventilatory/Hypercapneic failure

Hypoxemic failure (most commonly V/Q mismatch ± Shunt regions):

- Alveolar filling processes (e.g., blood, pus, or water)
 - e.g., pneumonia, CHF, alveolar hemorrhage
- Restrictive lung disease (can also cause hypercapnea)
 - Parenchymal: e.g., pulmonary fibrosis, drug-induced pneumonitis
 - Chest wall: e.g., post-thermal injury eschar, morbid obesity, abdominal compartment syndrome

Hypercapneic failure

- "Won't Breathe": central nervous system derangement, sedation
- "Can't Breathe": COPD, status asthmaticus, neuromuscular weakness
- Excessive physiologic *Dead Space*; significant concern for inability to wean with 60% or higher dead space fraction

Ventilator Management, Specific scenarios (while treating the underlying cause of respiratory failure):

- Ventilator Management for Hypoxemic Respiratory Failure
 - Alveolar filling processes: see Chapter 5 on ARDS
 - \bullet Avoid over-distention and aim tidal volumes 6 cc/kg and try to keep plateau pressures <30 cm $\rm H_2O$
 - PEEP can redistribute fluid from alveolar to interstitial spaces and can, therefore, be beneficial in CHF, alveolar hemorrhage
 - Restrictive lung disease:
 - Relieve restriction if possible (e.g., escharotomy, abdominal surgery, etc.)
 - Avoid over-distention especially in interstitial lung disease; higher PEEP application in stiff lungs can worsen physiologic dead-space via compressing adjacent alveolar capillaries and creating areas of "high" V and "low" Q (see V/Q figure above)
- Ventilator Management for Hypercapneic Respiratory Failure
 - "Won't Breathe"
 - Careful not to over-ventilate
 - Tube often in place for airway protection until underlying cause can be reversed

- "Can't Breathe" (e.g., airflow obstruction or neuromuscular weakness)
 - COPD: May have higher baseline PaCO₂ and should aim not to ventilate below this if possible to facilitate future weaning
 - If treating non-intubated patient, DO NOT deprive patient of adequate oxygenation because of fear of hypercapnia. Can limit O₂ supplementation to achieve sats of 90%–92%. If hypercapnea develops, may need to assist ventilation by Noninvasive Ventilation (NIV) or intubation
 - In intubated patient: concern for exacerbation of hyper-inflation and auto-PEEP.
 - Watch for incomplete exhalation and development of auto-PEEP: can consider decreasing RR, TV, and/or increasing flow rates to increase exhalation-time
 - Watch BPs closely, as some patients with COPD may have developed pulmonary hypertension and/or cor pulmonale and therefore be more likely to be hypotensive with intubation, positive pressure in general from the ventilator, and application of PEEP
 - Consider antibiotics for COPD flares in sick patients
 - Consider earlier extubation to NIV
- Asthma: might need to tolerate high peak pressures in order to deliver sufficiently high flows in light of airway resistance and need for adequate exhalation time to avoid air-trapping
 - Medications to consider: steroids, b-agonists
 - Also can consider Heliox (Helium—oxygen mixture; lower-density gas converts turbulent to laminar flow predominantly in larger airways but might also have benefit in smaller airways in asthma and/or through improving albuterol deposition in smaller airways, though debated)
- Neuromuscular weakness look for reversible causes; provide adequate nutrition; consider early tracheostomy if underlying process isn't quickly reversible

Sedation, Analgesia, and Neuromuscular Blockade for Mechanically Ventilated Patients (Crit Care Med. 2008;36:296) (see Chapter 8)

Community Acquired Pneumonia and Atypical Pneumonias (Clin Infect Dis. 2007;44:S27)

Site of care: Admission to the ICU is recommended for patients with either of the Major Criteria, or at least 3 Minor Criteria:

- Major Criteria: 1. Invasive Mechanical Ventilation
 - 2. Septic shock with need for vasopressors
- Minor Criteria: Respiratory Rate ≥30 breaths/min; PaO₂/F_IO₂ ratio ≤250; Multi-Lobar infiltrates; Confusion; Uremia; Leukopenia; Thrombocytopenia; Hypothermia; Hypotension (requiring IV fluids)

Diagnostic Testing and Treatment: diagnosis is established with suggestive clinical features (e.g., cough, fever, sputum, pleuritic chest pain) and supported by chest radiography demonstrating an infiltrate.

- For patients requiring ICU admission, the following testing is recommended, although testing should not delay early broad spectrum antibiotic administration, as each hour of delay in appropriate antibiotics has been associated with increased mortality:
 - Blood cultures
 - Sputum cultures (if intubated, endotracheal tube aspirate and consider bronchoscopy depending upon clinical situation)
 - Legionella urinary antigen test
 - Pneumococcal urinary antigen test (highly sensitive)
 - If pleural effusion present, consider thoracentesis and pleural fluid cultures
 - During outbreaks, isolation and rapid testing is recommended for Influenza
- For other subpopulations of patients, additional diagnostic and therapeutic approaches should be considered (see Table)

Types of Pneumonia and Pathogens				
Host	Likely Pathogens	Additional Testing	Empiric Treatment	
"Normal" ICU host within 48 hr of hospi- tal/ICU admis- sion	"Typical Bacterial Pathogens": Strep. pneumoniae, Hemoph. influenzae, Moraxella catarrhalis; "Atypical Bacterial Pathogens": Chlamyd. pneumoniae, Mycoplasma pneumoniae, Legionella pneumo- philia; Viral Pathogens: influenza	See above; "atypical pathogens" may be difficult to detect and therefore empiric treatment must be considered especially in absence of detecting another pathogen	β-lactam and fluo- roquinolone; con- sider oseltamivir during influenza season	

Hospital/ICU- acquired (>48 hr of hospitaliza- tion); ventilator- associated pneu- monia (fever, new infiltrate, increased secre- tions)	Above pathogens for "Normal host", plus Gram negative bacilli and Methicillin-Resistant Staphylococcus Aureus (MRSA)	Consideration of bronchoscopy if no pathogen iso- lated from sputum and not improving	Addition of 3rd generation cephalo- sporin with anti- pseudomonal activity and Vancomycin (for MRSA coverage)
Severe COPD, chronic steroid use, chronic or frequent antibiotic use, alcoholism	High risk for pseudo- monas and other gram- negative pathogens; patients on chronic ste- roids at risk for atypical infections including PCP, nocardia, semi-invasive aspergillosis	Consider CT chest for additional evaluation for structural lung disease, abscess; sputum for PCP (and serum β-D-glucan and LDH); modified AFB stain, nocardia culture, fungal stain/culture, serum galactomannan (to look for invasive aspergillus)	Coverage as above for hospital/ICU acquired infection, plus consideration of other pathogens listed based upon clinical presentation; consideration of anaerobic coverage if aspiration event suspected
Neutropenic host	In addition to hospital- acquired organisms, increased risk for fungal infections; for viral pathogens (RSV, adeno- virus, parainfluenza)	Rapid viral panel from nasal swab; Sputum for fungal stain and fungal culture; Blood β-D-glucan and galactomannan (for fungus and aspergillus)	For neutropenic fevers, anti-pseudo- monal 3rd genera- tion cephalosporin; consider broader coverage (anti- fungal if persistent fevers)

PCP, Pneumocystis carinii pneumonia (also known as pneumocystis jirovecii); LDH, lactate dehydrogenase; AFB, acid-fast bacilli; RSV, respiratory syncytial virus; MRSA, Methicillin-resistant staphylococcus aureus.

Duration of antibiotic treatment:

- Antibiotics should be narrowed to cover identified pathogens after ~48 hr of culture growth
- Definitive data is lacking, but in ICU patients with severe pneumonia, an 8-day course is reasonable if clinical response is observed, unless infection is documented with non-fermenting gram-negative rods (e.g., *Pseudomonas aeruginosa*), for which a 15-day course is more effective (*JAMA*. 2003;290:2588).

Non-responding pneumonia:

- As many as 15% of patients with CAP (and perhaps larger % of patients with impaired immune systems) may not respond to initial treatment, and as many as 40% of patients admitted to an ICU with pneumonia may worsen after initial stabilization (e.g., within 72 hr)
- Causes of failure to improve, or worsen:
 - Wrong antibiotics (e.g., missed pathogen or resistant organism)
 - Reculture, re-check existing culture data/sensitivities
 - Consider bronchoscopy/bronchoalveolar lavage
 - Extension of infection and/or complicated infection
 - Local (e.g., parapneumonic effusion, empyema, lung abscess, development of ARDS)
 - Distant (e.g., bacteremia, endocarditis, brain abscess)
 - Consider CT chest, echocardiogram, additional imaging based upon symptoms (e.g., abdominal CT)
 - Wrong diagnosis or missed additional process (e.g., PE, CHF, vasculitis, etc.)

- Consider echocardiogram, serologies (e.g., ANCA, ANA), lower extremity ultrasound to r/o DVT and/or CT angiography if renal function allows and clinical scenario consistent to evaluate for PE
- Nosocomial superinfection (e.g., VAP, Clostridium Difficile, central venous catheter infection)
 - Consider changing indwelling catheters, check stool *C. Difficile*, RUQ ultrasound to rule-out acalculous cholecystitis, amylase/lipase in consideration of pancreatitis
- Adverse reaction to medication (e.g., drug fever, anaphylaxis)
 - Consider discontinuing unnecessary antibiotics and/or changing class of antibiotics

Prevention:

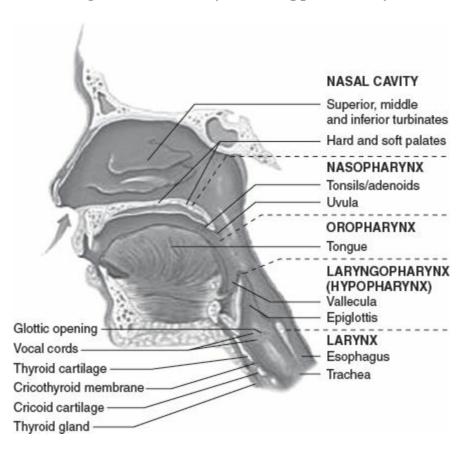
- Consider vaccination with pneumovax and influenza vaccines at hospital discharge or in the outpatient setting (as most patients with pneumonia requiring ICU admission will likely be candidates for vaccination)
- Smoking cessation resources should be offered to patients who smoke

AIRWAY MANAGEMENT

TARUN BHALLA, MD • TENSING MAA, MD • AMOD SAWARDEKAR, MD

Airway I	nnervation - Sensory
Glossopharyngeal Nerve (CN IX) Posterior 1/3 of tongue, oropharynx from pharyngeal surface to junction of p	
Superior Laryngeal Nerve, internal branch (CN X/Vagus)	Mucosa from epiglottis to vocal cords (sensory innervation of larynx above vocal cords), including base of tongue, supraglottic mucosa, cricothyroid joint
Superior Laryngeal Nerve, external branch (CN X/Vagus)	Anterior subglottic mucosa
Recurrent Laryngeal Nerve (CN X/ Vagus)	Subglottic mucosa, muscle spindles
Trigeminal Nerve (CNV)	Nares and nasopharynx

Figure 1. Anatomy of the Upper Airway



Airway Innervation – Motor			
Superior Laryngeal Nerve, external branch (CN X/Vagus)	Cricothyroid muscles tensing of vocal cords, inferior pharyngeal constrictors		
Recurrent Laryngeal Nerve (CN X/Vagus)	All other intrinsic muscles of larynx: thyroarytenoid, lateral cricoarytenoid, interarytenoid, posterior cricoarytenoid		
Glossopharyngeal (CN IX) and Superior Laryngeal, Internal Branch (CN X/Vagus)	No motor innervation contribution		

Note: all laryngeal motor innervation is by 2 branches of vagus: superior laryngeal n. and

recurrent laryngeal n.

- Injury of SLN (external branch) → hoarseness
- Injury of RLN: unilateral paralysis → paralysis of ipsilateral vocal cord → hoarse voice; bilateral paralysis → stridor and respiratory distress

Airway Assessment

- History:
 - Adverse events related to prior airway management
 - Radiation/surgical history
 - Burns/swelling/tumor/masses/facial or airway trauma
 - Obstructive Sleep Apnea (snoring)
 - Temporomandibular joint dysfunction
 - Dysphagia
 - Problems with phonation
 - C-spine disease (disk dz, osteoarthritis, rheumatoid arthritis, Down's syndrome, ankylosing spondylitis)
 - Congenital syndrome (Trisomy 21, Pierre Robin, Treacher Collins)
- Physical Examination
 - Position of comfort (tripoding?)
 - Level of consciousness
 - Respiratory mechanics: RR and regularity, head bobbing, grunting, flaring, accessory muscle use, wheeze or prolonged exhalation
 - Edema, upper airway trauma
 - Mallampati score
 - Symmetry of mouth opening (3 finger breadths)
 - Loose/missing/cracked/implanted teeth
 - Macroglossia (associated with difficult laryngoscopy)
 - High arched palate (associated with difficulty visualizing larynx)
 - Mandible size:
 - Thyromental distance <3 fingerbreadths suggests poor laryngeal visualization
 - Neck Examination
 - Cervical spine injury or instability
 - Prior surgeries/tracheostomy scars
 - Abnormal masses (hematoma, abscess, goiter, tumor) or tracheal deviation
 - Neck circumference and length
 - Range of motion (flexion/extension/rotation)

Mn	emonic for Airway Evaluation (LE	MON)	
Physical Signs	Signs of a Potentially Difficult Airway		
Look externally	Abnormal face shape Sunken cheeks Edentulous "Buck teeth"	Narrow mouthObesityReceding mandibleFacial/neck pathology	
Evaluate the 3-3-2 rule	 Mouth opening <3 fingerbreadths Hyoid-chin distance <3 fingerbreadths 	Thyroid cartilage-mouth floor distance <2 finger- breadths	
M allampati	Class III and IV	30.00-00-00-00-00-00-00-00-00-00-00-00-00	
Obstruction	Pathology around upper airway (peri-tonsillar abscess)		
Neck Mobility	Limited range of motion		

Airway Devices

- Oral and Nasal Airways
 - Typically inserted to relieve upper airway obstruction due to loss of upper airway muscle tone in obtunded/semi-conscious patients → usually caused by tongue or epiglottis falling against posterior pharynx wall
 - Size of oral airway estimated by measuring from corner of mouth to angle of the mandible
 - Length of nasal airway estimated by measuring from nares to tragus of ear
 - Use extreme caution with insertion in pts on anticoagulation or with basilar skull fractures
- Mask Airway
 - Facilitate O₂ delivery using airtight seal
 - Hold mask with left hand, while right hand generates positive pressure ventilation \rightarrow (use <20 cm H_2O to avoid gastric inflation). Confirm that mask ventilation is effective by checking for chest rise and/or by confirming breath sound with auscultation
 - Single person, "E-C clamp" technique
 - Fit snugly around bridge of nose to below bottom lip
 - Elicit downward pressure with left thumb and index finger ("C"), have the middle and ring fingers grasp the mandible, while the 5th finger is placed under angle of jaw to thrust anteriorly ("E")

Difficult Mask Ventilation: Maneuvers to Maintain Airway Patency

- Call for additional help to assist with 2-person bag mask ventilation (have someone else squeeze bag)
- Insert oral and or nasal airways
- · Extend neck and rotate head
- Perform jaw thrust

Independent Risk Factors for Difficult Mask Ventilation

- Presence of a beard
- Body mass index >26 kg/m²
- · Lack of teeth
- Age >55
- History of Snoring

(Langeron: Prediction of difficult mask ventilation, Anesthesiology. 92:1229, 2000)

- Supraglottic Airways (Laryngeal Mask Airways or LMAs)
 - Insertion technique:
 - Patient placed in sniffing position
 - Deflated LMA is lubricated and inserted blindly into hypopharynx (note that many operators insert the LMA while it is inflated, finding it easier to displace the tongue and soft tissues with an inflated LMA)
 - Cuff is inflated to create a seal around entrance to larynx (*tip rests over upper esophageal sphincter*, *the cuff's upper border rests against the base of tongue, sides lying over pyriform fossae*)
 - Indications:
 - Alternative to endotracheal intubation (not as a replacement) or mask ventilation
 - Rescue device in expected/unexpected difficult airway
 - Conduit for intubating stylet, flexible fiberoptic bronchoscopy/intubation (FOB), or small diameter endotracheal tube (ETT)
 - Contraindications:
 - Pharyngeal pathology, obstruction, high aspiration risk, low pulmonary compliance (need peak inspiratory pressures >20 cm H₂O), long surgeries
 - Disadvantages: does not protect the airway, can become dislodged
 - Endotracheal Tubes
 - Modified for a variety of specialized applications:
 - Flexible, spiral-wound, wire-reinforced (armored), rubber, microlaryngeal, oral/nasal RAETM (preformed), double lumen tubes
 - Airflow resistance depends on tube diameter, curvature, length
 - All endotracheal tubes have an imprinted line that is opaque on radiographs

Oral Tracheal Tube Sizing			
Age	Internal Diameter (mm)	Tube Length at Lip (cm)	
Full Term Infant	3.5	12	
Child	4 + Age/4	14 + Age/2 or 3 × ETT diameter	
Adult: Female Male	7.0–7.5 7.5–8.5	20 22	

- Rigid Laryngoscopes: used to examine larynx and facilitate tracheal intubation
 - Macintosh blade (curved): tip inserted into vallecula; use size 3 blade for most adults
 - Miller blade (straight): tip inserted beneath laryngeal surface of epiglottis; use 2 blade for most adults
 - Modified laryngoscopes: Wu, Bullard, and Glidescope for use in difficult airways
- Flexible Fiberoptic Bronchoscopes
 - Indications: potentially difficult laryngoscopy/mask ventilation, unstable cervical spines, poor cervical range of motion, TMJ dysfunction, congenital/acquired upper airway anomalies
- Light Wand
 - Malleable stylet with light emanating from distal tip, over which ETT is inserted
 - Dim lights in OR and advanced wand blindly
- C-MAC: newly available direct laryngoscopes using fiberoptics with larger display screens and slightly different configuration of blades are improving the visualization of airway for patients who are otherwise difficult to intubate

- Glow in lateral neck → tip in piriform fossa
- Glow in the anterior neck → correctly positioned in trachea
- Glow diminishes significantly → tip likely in esophagus
- Retrograde Tracheal Intubation
 - Performed in awake and spontaneously ventilating pts
 - Puncture cricothyroid membrane with 18G needle
 - Introduce guide wire and advance cephalad
 - Visual wire with direct laryngoscopy and guide ETT through vocal cords
- Airway Bougie
 - Solid or hollow, semi-malleable stylets usually passed blindly into trachea
 - ETT is threaded over bougie into trachea; can feel "clicking" as passes over tracheal rings
 - May have internal lumen to allow for insufflation of O₂ and detection of CO₂
- Recently the Aintree catheter (Cook Medical), a special Bougie, has become available. It is hollow on the inside and accommodates a pediatric fiberoptic bronchoscope so it can be placed into the trachea under direct fiberoptic visualization. Then, subsequently, it can be used as a tube guidance device (Bougie) to place the ETT over it.

Required Equipment for Intubation	
O ₂ , positive pressure ventilation source (ventilator) and back-ups (bag-valve mask)
Face masks, oropharyngeal and nasopharyngeal airways	
Endotracheal tubes (cuffed and uncuffed, 1 size up and 1 size down) and stylets	
Syringe for tracheal tube cuff inflation (10 ml)	
Suction	
Laryngoscope handles and blades (with functioning lights)	
Towel, blanket for pt positioning	
Stethoscope, capnograph or end tidal CO ₂ detector	

Indications for Tracheal Intubation

- Upper airway obstruction
- Emergency drug delivery in cardiac arrest (epinephrine, atropine, lidocaine, naloxone)
- Respiratory failure
- Shock or hemodynamic instability
- Neuromuscular weakness with progressive respiratory compromise
- Absent protective airway reflexes (cough, gag)
- Inadequate respiratory drive
- Need to maintain normocarbia in patients with increased ICP

Drugs

- Local anesthetics
 - 1%–4% lidocaine, cocaine solution, phenylephrine + lidocaine for vasoconstriction and anesthesia prior to nasal intubations
- Analgesia
 - Fentanyl, morphine
 - Synergistic effects on respiratory depression when given with a benzo
- Sedation
 - Benzodiazepine
 - Midazolam, lorazepam

- Synergistic effects on respiratory depression when given with an opiate
- Barbiturates
 - Thiopental (not avail. in US) decreases cerebral oxygen consumption and reduces ICP, also negative inotropy, hypotension
- Etomidate decreases cerebral oxygen consumption and reduces ICP, few CV side effects, adrenal suppression, lowers seizure threshold
- Propofol negative inotropy, vasodilation
- Dissociative anesthesia (Ketamine) analgesia and amnesia
- Muscle relaxants
 - Succinylcholine a depolarizing muscle relaxant, may cause bradycardia in infants, due to its effects on the muscarinic acetylcholine receptors; contraindicated in hyperkalemia, history of trauma, burns, crush injuries, neuromuscular disease (may cause or worsen hyperkalemia), caution in acute renal failure or chronic renal insufficiency if K is elevated, causes temporary elevation of intra-cerebral and intra-occular pressures (avoid if elevated ICP or globe injury; can trigger malignant hyperthermia
 - Nondepolarizing agents (rocuronium, vecuronium, cis-atracurium, pancuronium)

	Pre-ind	luction Agents	
Agent	Indication	Dose (IV)	Comments
Atropine	Prevents bradycardia during laryngoscopy	0.01-0.02 mg/kg (min 0.1 mg)	For children <1 yr
Glycopyrrolate	Prevents bradycardia and decrease oral secretions	3–5 mcg/kg	
Lidocaine (iv or via ETT)	Blunts HTN and ICP response with laryn- goscopy and broncho- spasm due to insertion of ETT	1–1.5 mg/kg	Give 3—4 minutes prior to laryngoscopy
Fentanyl	Analgesia, blunts increase HR and BP during laryngoscopy	2–3 mcg/kg	Rigid chest syndrome, rarely bradycardia
Esmolol	Blunts increase in HR and BP during laryn- goscopy	2 mg/kg	Caution in hemody- namically unstable patients

		Induction Agents	
Agent	Dose (IV)	Indications	Precautions
Thiopental (not avail. in US)	3–5 mg/kg	Status epilepticus, elevated ICP	Bronchospasm, hypotension
Etomidate	0.15-0.3 mg/kg	Trauma, hemodynamic instability	Adrenal suppression, lowers seizure threshold
Ketamine	1–2 mg/kg	Status asthmaticus, hemodynamic instability	May increase ICP, apnea, laryngo- spasm, hypersalivation
Propofol	2-4 mg/kg	Elevated ICP	hypotension
Midazolam	0.1-0.2 mg/kg	Amnesia, sedation	hypotension
Fentanyl	5-10 mcg/kg	Analgesia, hemody- namic instability	Rigid chest syndrome
Morphine	0.1 mg/kg	Analgesia	Histamine release, hypotension

Neuromuscular Blockade					
Agent	Class	Dose (IV)	Comments		
Succinylcholine	DNMB	1-1.5 mg/kg	See above		
Rocuronium	NDNMB	1-1.2 mg/kg	Hepatobiliray excretion		
Cis-atracurium	NDNMB	0.1 mg/kg	Hoffman degradation		
Vecuronium	NDNMB	0.1 mg/kg	Hepatobiliary excretion		

DNMB, depolarizing neuromuscular blocker; NDNMB, non-depolarizing neuromuscular blocker.

Airway Management: Orotracheal Intubation

- Gather all anticipated equipment and drugs including bolus IVF (hypotension associated with changes in intrathoracic pressure in critically ill patients)
- Elevate height of bed to laryngoscopists xyphoid process
- Place patient in *Sniffing Position*: neck flexion, head extension; aligns oral, pharyngeal, and laryngeal axes to provide the straightest view from lips to glottis
- Preoxygenation with 100% O_2 (a true de-nitrogenation step, replacing nitrogen with 100% oxygen) to increase the safe apnea period
- Induce anesthesia
- Hold laryngoscope in left hand, scissoring mouth open with right thumb and index finger
 - → insert laryngoscope in right side of mouth, sweeping tongue to left
 - → advance until glottis appears in view
 - → do not use laryngoscope as a lever in a pivoting maneuver (instead lift "up and away")
- Using the right hand pass the tip of the ETT through vocal cords under direct visualization
- Inflate ETT cuff with least amount of air necessary to create seal during positive pressure ventilation
- Confirm correct placement of ETT with: 1) Chest auscultation, 2) ETCO₂, 3) Palpate ETT cuff in sternal notch, 4) may use fiberoptic bronchoscopy to confirm endotracheal placement of ETT *Earliest manifestation of bronchial intubation is* ↑ *peak pressure* (*R. mainstem bronchus common*)

For trauma airway management, see Trauma and Bedside Procedures (Chapters 15 and 40)

- Rapid Sequence Intubation
 - Indication: pts at ↑ risk for aspiration
 - (full stomach, pregnant, GERD, morbidly obese, bowel obstruction, delayed gastric emptying pain/diabetic gastroparesis)
 - Use rapid paralyzing agent: succinylcholine (1–1.5 mg/kg) or rocuronium (0.6–1.2 mg/kg)
 - Place cricoid pressure (Sellick Maneuver) as pt is induced
 - protect regurgitation of gastric contents to oropharynx
 - help visualize vocal cords during laryngoscopy
 - Proper cricoid pressure should be performed with "BURP" technique:
 - displace larynx (B)ackward, (U)pward, (R)ight, with (P)ressure
 - Intubate pt once paralytic takes effect (30–60 secs); do **not** mask ventilate pt
 - Release cricoid pressure once ETT placement into airway is confirmed

Airway Management: Nasotracheal Intubation

- Indications: intraoral, facial/mandibular procedures
- *Contraindications:* basilar skull fractures, nasal fractures, polyps or tumors, underlying coagulopathies, upper airway foreign body obstruction

- *Preparation:* anesthetize and vasoconstrict mucosa with lidocaine/phenylephrine mix or cocaine → select nares that pt can breath through most easily
- Lubricated ETT is advanced perpendicular to face below inferior turbinate via selected nares → direct bevel laterally away from turbinates
- Advance ETT until able to visualize tip in oropharynx under direct laryngoscopy → use Magill forcep with right hand to advance/direct through vocal cords

Airway Management: Awake Flexible Fiberoptic Intubation

- *Equipment:* ovassapian/Willliams/Luomanen airway, topical anesthetics, vasoconstrictors, antisialagogues, suction, fiberoptic scope with lubricated ETT
- *Indications:* cervical spine pathology, obesity, head and neck tumors, hx of a difficult airway, presence of anterior mediastinal mass
- Premedication: sedation (midazolam, fentanyl, dexmedetomidine, ketamine)
- Technique:
 - 1) take time to topicalize airway while continuing to preoxygenate
 - 2) place special oral airway or grab tongue with gauze
 - 3) Keep fiberoptic scope in midline while advancing until epiglottis appears
 - 4) Advance scope beneath epiglottis using antero/retroflexion as needed
 - 5) Once vocal cords are visualized, advanced scope into trachea
 - 6) Stabilized scope while ETT is advanced off scope into trachea → if resistance is encountered, rotate ETT tube 90 degrees
 - 7) After insertion, visualize carina with scope to avoid endobroncial intubation

ASA Difficult Airway Algorithm

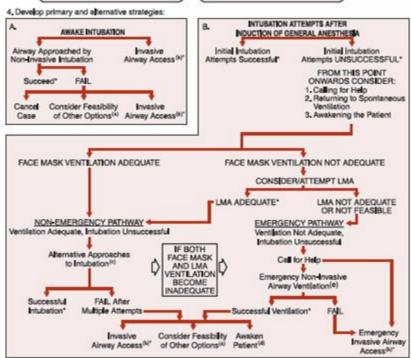
Neuromuscular Blockade



DIFFICULT AIRWAY ALGORITHM

- 1. Assess the Ikelihood and clinical impact of basic management problems:
 - A. Difficult Ventilation
 - B. Difficult Intubation
 - C. Difficulty with Patient Cooperation or Consent
 - D. Difficult Tracheostomy
- 2. Actively pursue opportunities to deliver supplemental oxygen throughout the process of difficult airway management
- 3. Consider the relative merits and feasibility of basic management choices:





"Confirm ventilation, traches intubation, or LMA placement with exhaled CO₂

- Other options include (but are not limited to); surgery utilizing face mask or LMA anesthesis, local anesthesis infiltration or regional nerve tipockade, Pursuit of these options usually implies that mask vertilation will not be proclemate. Therefore, these options may be of limited value if this step in the algorithm has been reached via the
- the Emergency Pathway, b. Invasive alreay access includes surgical or percutaneous truchesstomy or cricolhyrolomy.
- n-invasive approaches to difficult intubation include c. Azernative non-immusere appresence to amous imposton induce (but are not firmited to); use of different layingoscope blades, UMA as an intubation conduit (with or without fiberoptic guidance), theroptic initiation, initiating syllet or tabe change, light wand, netrograde initiation, and blind one or nasal initiation, d. Consider re-preparation of the patient for awake initiation or
- Consider represen-canceling surgery.
 Options for emergency non-invasive einesy ventilation include (but are not limited to); rigid bronchoscope, ecophageol-trached combitube ventilation, or transtrached jet ventilation.

	Practical Approach to Unanticipated Difficult Airway	
Plan A	 Standard laryngoscopy with blade of choice If unable to intubate → make 2nd attempt with a different blade Make no more than 2 attempts (avoid ↑ risk of oral bleeding, secretions, and edema) 	
Plan B	 Direct laryngoscopy and insertion of bougie or intubating catheter Confirm placement by: Using hand on anterior neck to palpating catheter advancement through glottis After 40 cm catheter should reache carina and provide resistance (no resistence will be encountered if in esophagus) If using intubating catheter, may attach to ETCO₂ monitor 	
Plan C	 Insertion of LMA (disposable, fasttrach, proseal) 5.0 or 6.0 ETT will fit through disposable LMA (± fiberoptic assistance) 	

Plan D If intubation attempts are unsuccessful and it is safe to do so: Terminate anesthetic and awaken patient Perform awake fiberoptic intubation Perform surgical airway (i.e., tracheostomy) Plan E If intubation attempts are unsuccessful and the patient cannot be safely woken up from anesthesia have a qualified person (usually surgeon) perform a tracheostomy or cricothyroidotomy to secure the airway

Transtracheal Procedures

- Indications: emergency tracheal access when an airway cannot be secured via nasal/oral route
- Percutaneous transtracheal jet ventilation
 - Simple and relatively safe means to sustain a patient during a critical situation
 - Attach 12, 14, or 16 gauge iv catheter to 10 cc syringe with partially filled saline
 - Advance needle through cricothyroid membrane with constant aspiration, until air returns
 - Advance angiocatheter, disconnect syringe, attach oxygen source
 - High press O_2 (25–30 psi), insufflation of 1–2 secs, 12/min with 16 gauge \rightarrow will deliver approximately 400–700 ml
 - Low pressure O₂ (Bag-valve mask 6 psi, common gas outlet 20 psi)

• Cricothyroidotomy (must be performed by a qualified practitioner experienced with the procedure)

- Contraindications: patients <6 yrs old (upper part of trachea not fully developed)
- → incision through cricothyroid membrane ↑ risk of subglottic stenosis
- Sterilize skin
- Identify cricothyroid membrane
- Transverse incision with #11 blade \approx 1 cm on each side of midline
- Turn blade 90° to create space to pass ETT
- Insert ETT caudally, inflate cuff, confirm breaths sounds

Tracheotomy (must be performed by a qualified practitioner experienced with the procedure)

Indications: prolonged tracheal intubation, neurologic impairment, congenital airway malformations, craniofacial syndromes, vocal cord paralysis

Complications:

- Immediate post-op: tube occlusion, accidental decannulation, false passage, pneumomediastinum, pneumothorax
- Late: laryngeal stenosis, tracheal stenosis, stomal granuloma formation, stomal bleeding, tube occlusion, infection, innominate artery erosion

Complications of Laryngoscopy and Intubation (most common)

- **Post-intubation stridor** in children 2° to tracheal/laryngeal edema, treat with decardon periextubation and racemic epinephrine or decadron nebs post-extubation, heliox, humidified oxygen
- Acquired subglottic stenosis in children from incorrect tracheal tube size, traumatic or multiple intubations, inadequate sedation/analgesia resulting in excessive ETT movement and trauma to airway
- Recurrent laryngeal nerve damage from ETT cuff compression → vocal cord paralysis
- Laryngospasm from stimulation of superior laryngeal n.
 - Involuntary/uncontrolled muscular contraction of laryngeal cords
 - Caused by pharyngeal secretions or direct stimulation of ETT during extubation
 - Treat with:
 - 1) gentle positive pressure ventilation
 - 2) laryngospasm maneuver-apply firm pressure posterior to mandibular ramus near the earlobe
 - 3) succinylcholine 0.25-1 mg/kg to relax laryngeal muscles

• Nosocomial Infection (ventilator associated pneumonia (see Chapter 10))

Extubation

- Extubation readiness patient factors:
 - Resolution of initial indication for intubation,
 - Adequate gas exchange capacity,
 - Airway protective reflexes, (cough, gag),
 - Respiratory muscle strength (NIF, VC), spontaneous breathing trial,
 - Sedatives weaned for adequate respiratory drive and muscle relaxants reversed,
 - Adequate cardiac function to tolerate increase in LV afterload
- \bullet Patients airway should be aggressively suctioned while on 100% O_2 prior to extubation
- Consider cuff leak test: deflate cuff and listen for air leak to rule out glottic swelling and to decrease chance of post-extubation stridor (note: reliability of this test is controversial)
 - Consider delaying extubation if no leak
- Untape ETT, deflate cuff, remove ETT while providing small amount of positive pressure (remove secretions at distal end of ETT)
- Place mask on pt with 100% O2 while verifying spontaneous and adequate ventilation
- Negative-pressure pulmonary edema (Post-obstructive pulmonary edema, POPE)
 - Type 1 can occur during strong inspiratory effort caused by large negative intrathoracic pressure gradient against closed vocal cords
 - Type 2 can occur with relief of upper airway obstruction
 - Treatment: maintain airway, provide O₂, consider PEEP/reintubation, diuretics are used but are not very effective

ACUTE LUNG INJURY (ALI) AND ACUTE RESPIRATORY DISTRESS SYNDROME (ARDS)

JOHN J. O'CONNOR, MD • DANIEL S. TALMOR, MD

Introduction

- ALI/ARDS carries a mortality rate of approximately 38.5%
- Each year there are ~190,600 cases of acute lung injury (ALI) in the United States
- Many therapies have been investigated since Ashbaugh and colleagues described acute respiratory distress syndrome (ARDS) in 1967 and there continues to be ongoing research

PATHOPHYSIOLOGY

- ALI/ARDS is caused by capillary leak in the alveoli, and the disease process is likely related to the systemic inflammatory response syndrome (SIRS)
- Common predisposing conditions include sepsis, pneumonia, aspiration, pancreatitis, shock, and trauma
- Direct or pulmonary ARDS results from direct lung injury where as indirect or extra pulmonary ARDS may develop from other inflammatory disease states (like generalized infections or infections at sites other than the lungs)

Types of ARDS			
Direct ARDS	Indirect ARDS		
Pneumonia	Sepsis		
Trauma	Acute pancreatitis		
Aspiration	Burns		
Inhalational injury	Severe polytrauma		
Pulmonary contusion	Transfusion related acute lung injury (TRALI)		
Fat embolus	Cardiopulmonary bypass		
Amniotic fluid embolus			
Near drowning			

- There are three distinct pathologic stages of ARDS
 - Exudative: in early ARDS there is increased alveolar capillary permeability with neutrophil extravasation into the alveoli, resulting in diffuse alveolar damage and loss of pulmonary compliance
 - Fibroproliferative: beginning 1–2 wks after the onset of ARDS, some patients develop a fibroproliferative phase in the lung
 - Fibrotic: a few patients go on to develop pulmonary fibrosis

DIAGNOSIS

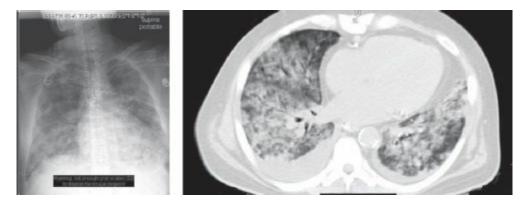
- In the past there have been several synonyms for ALI/ARDS, including congestive atelectasis, respirator lung, surfactant dysfunction, and non cardiogenic pulmonary edema
- Currently, ALI/ARDS are defined by the 1994 American-European Consensus Conference Criteria (AECC) for ALI and ARDS (*Am J Respir Crit Care Med.* 1994;149:818):

The Definition of ALI and ARDS				
ALI	ARDS			
CXR with bilateral patchy infiltrate	CXR with bilateral patchy infiltrate			
PaO ₂ to FiO ₂ ratio <300	PaO ₂ to FiO ₂ ratio <200			
Pulmonary capillary wedge pressure <18 cm H ₂ O or absence of clinical evidence of CHF	Pulmonary capillary wedge pressure <18 cm H ₂ O or absence of clinical evidence of CHF			
Acute onset and associated with one or more risk factors	Acute onset and associated with one or more risk factors			

- ALI can co-exist with congestive heart failure and clinical judgment is needed to differentiate
- A focused echocardiogram in the ICU setting can be helpful in ruling out left atrial hypertension as the cause of pulmonary edema
- Fergusen and colleagues have published an alternative criteria to address the deficiencies of the AECC definition; however, it has not gained widespread use:
 - $PaO_2/FiO_2 < 200$ with $PEEP \ge 10$
 - Onset <72 hrs
 - B/L airspace disease involving >2 quadrants of frontal CXR
 - No clinical evidence of CHF
 - Decreased lung compliance (<50 ml/cm H_2O in sedated patient with TV 8 ml/kg ideal body weight with PEEP ≥ 10
 - Predisposition, direct or indirect factor associated with lung injury

IMAGING

Figure 1. Chest Radiogram and CT Image of a Lung with ARDS



- The CXR shows bilateral patchy infiltrates
- The CT scan in the same patient shows bilateral infiltrates, areas of dependent atelectasis, and small pleural effusions. Such areas of lung are stiff and non-compliant
- There are also areas of undamaged lung tissue in the non-dependent regions
- Gattanoni et al. coined the term "baby lung" for these uninjured areas and postulated lower tidal

volume ventilation would prevent excessive mechanical forces on these areas of undamaged lung (Intensive Care Med. 2005;31:776)

TREATMENT

• There have been a number of attempts at pharmacologic therapy but currently the prevention of ventilator induced lung injury (VILI) is the mainstay of therapy

Prevention of Ventilator Induced Lung Injury

- The primary goal in lung protective ventilation is to prevent stress on undamaged alveolar units
- The four potential mechanisms of alveolar damage in patients with ARDS are:
 - Barotrauma: excessive airway pressures resulting in pneumothorax
 - Volutrauma: overdistention of alveoli from high tidal volume ventilation
 - Atelectrauma: shearing force on alveoli from opening during inspiration and collapse on expiration
 - Biotrauma: the release of pro-inflammatory cytokines from excessive mechanical forces on the lung
- In 2000, the National Heart, Lung and Blood Institute funded ARDS Network published a landmark study showing improvement in mortality with lung protective ventilation, specifically lower tidal volume ventilation, 6 cc/kg ideal body weight and plateau pressure limits of 30 mm Hg (N Engl J Med. 2000;342:1334)
- The ARDSnet data clearly show that low tidal volume ventilation is protective and demonstrated an absolute reduction in mortality of 9%

Permissive Hypercapnia

- Mechanical ventilation strategies that minimize tidal volume and plateau pressure can result in respiratory acidosis
- Current guidelines recommend maintaining PH above 7.30 and PaCO₂ in the 45–55 mm Hg range

Positive End Expiratory Pressure

- Positive end expiratory pressure (PEEP) both helps recruit atelectatic lung tissue and prevents the development of further atelectasis; it thereby improves ventilation—perfusion matching
- Although increased PEEP decreases hypoxemia it did not appear to improve survival in several trials
- Alternative methods of setting PEEP include using the lower inflection point of the pressure—volume curve, the stress index and titrating PEEP to a positive transpulmonary pressure estimated using an esophageal balloon catheter. Currently there is not enough evidence to recommend the routine use of these techniques.

Rescue Therapy

• Therapies that are not well proven but used for patients in extremis

Recruitment Maneuvers

• A typical recruitment maneuver is an attempt at re-expanding at electatic lung tissue by applying a constant positive pressure of about 30–40 mm H_2O for ~60 secs

• The routine use of recruitment maneuvers is not supported in the literature for ALI/ARDS patients

Positioning

- Oxygenation improves in 2/3 of patients when placed in prone position
- Prone positioning increases FRC by improving aeration of dorsal lung regions, unloads weight of heart
- Frequent turning has also been helpful in improving oxygenation in animal studies

Alternative Modes of Ventilation

- APRV:
 - Airway pressure release ventilation is a ventilation mode that maintains a constant airway pressure and promotes recruitment of alveoli
 - There are currently no studies showing a survival advantage but theoretically this strategy should promote recruitment of collapsed alveolar units
- High frequency oscillation:
 - May be useful for patients who have severe hypoxemia and have failed conventional ventilation
- Extra Corporeal Membrane Oxygenation:
 - There are ongoing studies in adults (currently has no proven benefit for adult ARDS patients)
 - Traditionally used in pediatric patients

Supportive Therapy

- Paralysis:
 - Initiating neuromuscular blockade in patients meeting ARDS criteria may be of benefit. In a recent study by Papazian and colleagues, the authors were able to show reduced mortality with the use of cisatracurium neuromuscular blockade for 48 hrs in patients diagnosed with early ARDS
 - The benefit is likely related to the ability to provide better lung protective ventilation
 - One concern regarding the use of neuromuscular blockers is the development of myopathy. However, there was no increase in myopathy in patients receiving neuromuscular blockers in this study (likely related to the short period of neuromuscular blockade: 48 hrs).
- Fluid management:
 - Conservative fluid management is beneficial. Positive fluid balance and increased extra vascular lung water is associated with poor outcomes.
- Nutrition:
 - Tube feeds with increased fat and decreased carbohydrates should theoretically result in less CO₂ production and decrease the amount of respiratory acidosis

Pharmacologic Therapy

- Anti-inflammatory agents/steroids:
 - Although inflammation is thought to be involved in the pathogenesis of ALI/ARDS, antiinflammatory therapies have been studied and have shown equivocal survival benefit
 - The use of corticosteroids in ALI/ARDS is controversial. Bernard and colleagues showed no difference in mortality in 1987; however, Meduri and colleagues showed a survival benefit with early initiation (<3 d of ARDS) of corticosteroids in a small randomized clinical trial.
 - In 2006, the ARDS Net Late Steroid Rescue Study looked at this and showed no survival benefit. In fact, the study showed increased mortality when steroids were started 14 d after the onset of ALI/ARDS.

- Steroids are currently not recommended as they have not consistently shown a survival benefit and present possible side effects to patients
- NSAIDS, statins, surfactant administration, ketoconazole (antifungal agent with anti-inflammatory properties that blocks leukotriene and thromboxane synthesis) have been studied and have shown no survival benefit in ALI/ARDS
- Inhaled nitric oxide:
 - Nitric oxide is an endogenous vasodilator that can improve pulmonary hypertension
 - No survival benefit has been demonstrated for ALI/ARDS patients
- Antiplatelet therapy:
 - There is new data indicating that anti-platelet medications may reduce the incidence of ALI/ARDS
 - Platelet activation is a key component of ALI/ARDS pathophysiology
 - In patients already on anti-platelet medications, Erlich and colleagues showed a decreased incidence of developing ARDS

OUTCOMES

- The incidence of hospital acquired ALI/ARDS has been decreasing over the past 10 yrs, and this has been attributed to improvements in the treatment of critically ill patients. However, the incidence of ALI/ARDS admitted from the community appears to be unchanged (*Am J Respir Crit Care Med.* 2011;183:59).
- Survival rates for ALI/ARDS are controversial. Some evidence suggests improved survival while a recent estimate of survival in the control groups of studies in ALI suggest that survival rates are unchanged (*Am J Respir Crit Care Med.* 2009;179:220)
- Most patients that survive have abnormalities on pulmonary function testing including muscle weakness, less distance walked in the standardized 6 min walk test, and in one study 6% had $\rm O_2$ saturation less than 88% with exercise
- A most recent study has found that 5 yrs after surviving ARDS the survivors had normal to near-normal results on their pulmonary function test, but they had significant exercise limitation with a decreased physical quality of life. As expected younger patients had a greater rate of recovery than older ones, but neither group returned to normal predicted levels of physical function at 5 yrs (*N Engl J Med.* 2011;364:1293).

CONCLUSION

- The mainstay of treatment for ALI/ARDS is lung protective ventilation combined with supportive intensive care
- Lung recruitment with PEEP and minimizing pulmonary edema with fluid restriction also appears to be helpful
- The management of ALI/ARDS related to infections (pneumonia) or sepsis should prioritize the timely and appropriate treatment of those infectious issues (see Chapter 10 for the specifics of the management of infections and sepsis)

HEMATOLOGY, FLUID AND ELECTROLYTE MANAGEMENT

YASSER EL KOUATLI, MD • LENA M. NAPOLITANO, MD

HEMATOLOGY

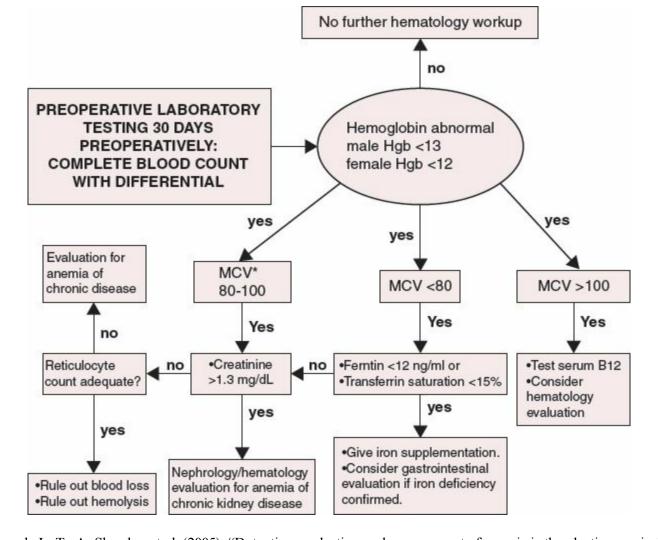
Anemia in the ICU

- Anemia is common in ICU patients, with >90% of patients with anemia on ICU day 3
- Anemia persists after ICU discharge, with >50% of patients still anemic 6 mos after ICU discharge
- Etiologies of anemia in the ICU include blood loss related to daily phlebotomy, hemodilution due to crystalloid fluid resuscitation, renal replacement therapies, renal disease, hemorrhage, occult blood loss from the gastrointestinal tract, bone marrow suppression due to diseases, drug-induced anemia, and nutritional deficiencies such as iron, folate, and vitamin B12 deficiency
- In ICU patients with anemia and chronic kidney disease, treatment with erythropoietin-stimulating agents (ESAs) is indicated, with target hemoglobin concentrations no higher than 9 g/dl. Adjunctive iron treatment should be strongly considered, as optimal response to ESAs requires supplemental iron.
- In most ICU patients, the etiology of anemia is "anemia of inflammation" or "anemia of chronic disease (ACD)"
- Anemia of inflammation develops via 3 mechanisms: (1) impaired iron regulation, (2) shortened RBC life span, and (3) reduced rate of erythropoiesis related to inappropriate erythropoietin response
- Hepcidin is the main iron regulatory hormone, made primarily in hepatocytes, and causes functional iron deficiency, hypoferremia and iron-restricted erythropoiesis despite normal iron stores by blocking enteral iron absorption and shuttling iron into macrophages where it is unavailable for erythropoiesis.
- Hepcidin concentrations are high in anemia of inflammation and ACD (*Intensive Care Med.* 2008 Sep–Oct;23(5):295)

Anemia: Clinical Approach to Diagnostic Evaluation

• ICU patients with anemia should undergo a diagnostic evaluation as for any patient with anemia (Figure 1).

Figure 1. Diagnostic Evaluation of Anemia



From: Goodnough, L. T., A. Shander, et al. (2005). "Detection, evaluation, and management of anemia in the elective surgical patient." *Anesth Analg.* 101(6):1858–1861.

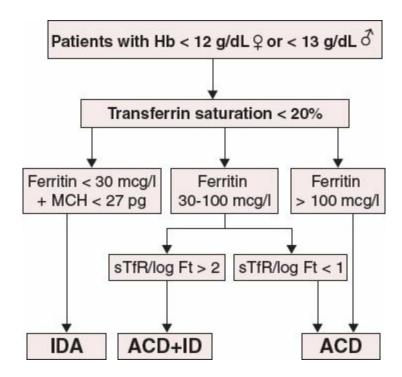
• Determination of the causative factors for anemia will allow appropriate anemia management which will aid in avoiding RBC transfusion solely for the treatment of anemia.

Anemia and Diagnosis of Iron Deficiency in the ICU

- Iron deficiency is difficult to diagnose in ICU patients since most will have high ferritin levels related to inflammation. In these patients, check zinc protoporphyrin which will be high in iron deficiency
- In the presence of inflammation true iron deficiency is defined by a ferritin <100 ng/ml and a TSAT < 20% (TSAT [transferrin saturation] is calculated by dividing the serum iron by the total iron-binding capacity [TIBC]), whereas functional iron deficiency is defined by ferritin >100 ng/ml and a TSAT < 20% (Figure 2).
- Total iron deficit (TID) can be calculated using the Ganzoni formula: TID (mg) = weight (kg) \times (ideal Hb actual Hb) (g/dl) \times 0.24 + depot iron (500 mg).
- According to this formula, a person weighing 70 kg with a Hb level of 9 g/dl would have a body iron deficit of about 1,400 mg. Following the administration of oral iron, it takes 2–2.5 wks for the Hb to start rising, 2 mos for it to return to normal levels, and 6 mos for iron stores to be replete.
- In Anemia of Inflammation or ACD, enteral iron absorption is problematic due to high hepcidin concentrations which block enteral iron absorption, and intravenous (IV) iron should be considered.

Figure 2. A Simplified Algorithm for the Diagnosis of Iron Deficiency Anemia (Modified from

Weiss and Goodnough (*N Engl J Med.* 2005;352(10):1011–23))



From: Muñoz M, García-Erce JA, Remacha AF. Disorders of iron metabolism. Part II: iron deficiency and iron overload. *J Clin Pathol*. 2011 Apr, 64(4):287–96.

ACD, anemia of chronic disease; Hb, hemoglobin; IDA, iron deficiency anemia; MCH, mean corpuscular hemoglobin; sTFR, serum transferrin receptor.

TRANSFUSION AND TRANSFUSION TRIGGERS IN THE ICU

Red Blood Cell (RBC) Transfusion

- RBC transfusion is common in ICU patients, with 40%–50% receiving RBC transfusion during the ICU stay
- The Transfusion Requirements in Critical Care (TRICC) Trial confirmed that ICU patient 30-day mortality was not different in patients randomized to a restrictive (transfuse if hemoglobin <7 g/dl) or liberal (transfuse if hemoglobin <10 g/dl) transfusion strategy. (*N Engl J Med.* 1999 Feb 11;340(6):409. Erratum in: *N Engl J Med.* 1999 Apr 1;340(13):1056)

Indications

- RBC transfusion for stable ICU patients without acute cardiac ischemia: guidelines recommend transfusion when hemoglobin <7 g/dl (see Guideline Executive Summary below).
- For ICU patients with acute cardiac ischemia: transfuse RBCs if hemoglobin <8 g/dl

Summary of Recommendations from Guidelines for RBC Transfusion in Adult Trauma and Critically III Patients A. Recommendations Regarding Indications for RBC Transfusion in the General Critically III Patient 1. RBC transfusion may be indicated for patients with evidence of hemorrhagic shock. (Level 1) 2. RBC transfusion may be indicated for patients with evidence of acute hemorrhagic shock. (Level 1) 3. A"restrictive" strangy of RBC transfusion (transfuse when Hb < 7 g/dl) is as effective as a "liberal" transfusion strategy (transfusion when Hb < 10 g/dl) in critically ill patients with hemodynamically stable anemia, secept possibly in patients with south produced in the patients of a "transfusion and extent of memia, and cardiopulmonary physiologic parameters. (Level 2) 4. The use of only Hb level as a "trigger" for transfusion should be avoided. Decision for RBC transfusion should be based on an individual patients's intravascular volume status, evidence of shock, duration and extent of memia, and cardiopulmonary physiologic parameters. (Level 2) 5. In the absence of acute hemocrhage RBC, transfusion should be given as single units. (Level 2) 6. Consider transfusion if Hb < 7 g/dl in critically ill patients requiring MY, (Level 2) 7. Consider transfusion if Hb < 7 g/dl in resistance critically ill transmapatients. (Level 2) 8. Consider transfusion if Hb < 7 g/dl in resistance critically ill transmapatients. (Level 2) 8. Consider transfusion if Hb < 7 g/dl in critically ill patients with stable cardiac disease. (Level 2) 9. RBC transfusion should not be considered as an absolute method to improve tissue coygen consumption in critically ill patients. (Level 3) 10. RBC transfusion may be beneficial in patients with stable cardiac disease. (Level 2) 10. RBC transfusion may be beneficial in patients with stable cardiac disease. (Level 2) 10. RBC transfusion meeds for each septic patient must be assessed individually since optimal transfusion in critically ill patients. (Level 3) 11. There are insuffic

D. Recommendations Regarding RBC Transfusion in Patients With Neurologic Injury and Diseases

1. There are insufficient data to support Level 1 Recommendations on this topic.

2. There is no benefit of a "liberal" transfusion strategy (transfusion when Hb < 10 g/dl) in patients with moderate-to-severe traumatic brain injury. (Lord 2)

3. Decisions regarding Blood transfusion in patients with subarchnoid hermorrhage (SAH) must be assessed individually since optimal transfusion triggers are not known and there is no clear evidence that blood transfusion is associated with improved outcome. (Level 3)

E. Recommendations Regarding RBC Transfusion Risks

1. There are insufficient data to support Level 1 Recommendations on this topic.

2. RBC transfusion is associated with increased no occomial infection (wound infection, pneumonia, sepsis) rates independent of other factors. (Level 2)

3. RBC transfusion is associated with increased no occomial infection (wound infection, pneumonia, sepsis) rates independent of other factors. (Level 2)

4. There is no definitive evidence that prestorage leukocyte depletion of RBC transfusion reduces complications. (Level 2)

5. RBC transfusions are independently associated with longer ICU and hospital length of stay, increased complications, and increased mortality. (Level 2)

6. There is a relationship between transfusion and ALI and ARDS. (Level 2)

7. Recommendations Regarding Alternatives to RBC Transfusion

1. There are insufficient data to support Level 1 recommendations on this topic.

2. Recommendations Regarding Strategies to Reduce RBC Transfusion

1. There are insufficient data to support Level 1 recommendations on this topic.

2. The use of blood conservation devices in the United States. (Level 2)

3. The use of blood conservation devices for reinfusion of waste blood with diagnostic sampling is associated with a reduction in phlebotomy volumes and a reduction in blood transfusion. (Level 2)

4. Interest and postoperative blood salvage and alternative methods for decrea

From: Napo Itano LM, et al. (2009) "Clinical practice guideline: red blood cell transfusion in adult trauma and critical care." Crit Core Med. 37(12):3124-3157.

Technical aspects

- ABO-Rh compatibility: RBC serology requires transfusion from patient with compatible ABO and Rhesus groups. In patient with multiple transfusion subgroup (A1, A2) and other groups (MN, K, D, L) compatibility becomes necessary.
- Crossmatched blood should be used unless unavailable or in emergent situations
- Temperature: re-warming blood products is a necessity as they are refrigerated for storage.
- Room temperature is acceptable for slow and low volume transfusions but using a blood warmer is necessary to prevent hypothermia if higher volume of blood products are transfused.
- Tubing and filters: blood tubing with a filter should be used for transfusions, the use of microfilters (pores of 30–40 micron) has not been associated with reduced complications.
- Monitoring during transfusions: patient vital signs including temperature should be monitored during and after completion of RBC transfusions.

In patients with bleeding or hemorrhagic shock:

- Use uncrossmatched blood (Type O) if pt has hemodynamic instability due to hemorrhagic shock
- Substitute type-specific blood for type O as soon as possible (in order to minimize exposure to anti-A & anti-B antibodies in type O blood)
- Transfusion rate depends on bleeding rate, do not rely on hemoglobin

Complications

- Citrate toxicity: metabolic alkalosis and hypocalcemia with low levels of ionized calcium in patients with impaired liver function or after massive transfusions.
- Electrolytes: low ionized calcium, hyperkalemia.
- Transfusion related febrile reactions.
- Anaphylactoid reactions
- Immunomodulation: with increased risk for infections
- Graft versus host disease
- Hemolytic reactions
- Transfusion related acute lung injury (TRALI)
- Infection: by contamination from donor (decreasing incidence) or contamination from manipulation (highest risk of infection with the transfusion of platelets stored at room temperature).
- Hypothermia
- Overall patient outcomes: many recent studies demonstrated worse outcomes in patients that were transfused in a critical care setting and perioperatively.

Fresh Frozen Plasma (FFP) Transfusion (Transfusion. 50(6):1227)

Indications

- FFP should be transfused to patients requiring massive transfusion.
- The optimal amount of FFP required in massive transfusion patients is controversial. The guidelines recommend plasma: RBC ratio of 1:3 or more during massive transfusion. Use coagulation studies and clinical evidence of bleeding as a guide.
- There is no recommendation for or against transfusion of plasma to patients undergoing surgery without massive transfusion.
- FFP should be transfused in patients with Warfarin therapy—related intracranial hemorrhage but could not recommend for or against transfusion of plasma to reverse Warfarin anticoagulation in patients without intracranial hemorrhage.
- The guidelines suggested against plasma transfusion for other selected groups of patients, including those with liver disease, Hemophilia (A&B), other factor deficiency and anti-thrombin deficiency in a situation requiring anticoagulation with heparin.

Technical aspects

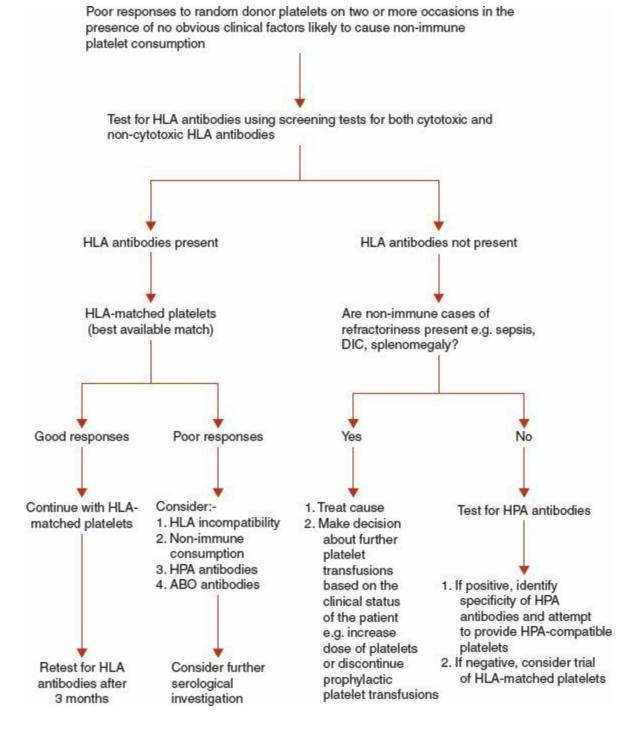
- Same technical aspects include using crossmatched plasma for transfusions in order to avoid a reaction between patient red blood cells and donor antibodies.
- ABO compatibility required, Rh compatibility not required

Complications

- Identical to RBC transfusion keeping in mind that citrate content is higher in FFP and potassium transfer is not an issue.
- TRALI has a higher incidence with plasma transfusions (particularly from multiparous female donors). Of note, the American Red Cross now only provides FFP from male donors to reduce the risk of TRALI.

Platelet Transfusion (Br J Haematol. 2003;122(1):10; Blood Rev. 12(4):239)

Figure 3. Diagnostic Evaluation for Thrombocytopenia Refractory to Platelet Transfusion



Indications

- Prophylactic platelet transfusions are indicated in patients at risk of bleeding, for platelet count $<10 \times 10^9/1$
- Therapeutic platelet transfusions are required in hemorrhage to keep platelet count $>100 \times 10^9/l$ required to create stable clot and minimize rebleeding
- In elective surgery, platelet transfusions may or may not be required, dependent on the procedure being performed
- Contraindications to platelet transfusions include thrombotic thrombocytopenic purpura (TTP) and heparin-induced thrombocytopenia (HIT)

Technical aspects

• Same as RBC transfusion with the necessity for ABO compatibility but RhD-negative platelet concentrates should be given, when possible, to RhD-negative patients and women in particular.

Complications

- Technical issues (related to platelet unit contamination and infection risk), platelet function (Deep venous thrombosis) and immune effects (alloimmunization and hemolysis from residual ABO antibodies).
- Some ICU patients will be refractory to platelet transfusions, defined as failure to achieve an appropriate increment after receiving 2 consecutive transfusions with fresh ABO-compatible platelets (Figure 3).

Measurement of platelet count 30 and 60 min following platelet transfusion will determine response.

Cryoprecipitate Transfusion (*Transfus Med Rev.* 23(3):177)

Indications

- Hypofibrinogenemia in the setting of massive hemorrhage.
- Second-line therapy for von Willebrand disease and hemophilia A (Factor VIII deficiency)

Technical aspects

Same as all blood products but ABO compatibility is not necessary.

Complications

Similar to all blood products and in case of large volume of ABO-incompatible cryoprecipitate is used, the recipient may develop a positive DAT and, very rarely, mild hemolysis.

Massive Transfusion

- Defined as ≥ 10 units RBC transfusion in 24 hr
- Associated with high mortality rates

Adverse effects of massive transfusion

• Hypocalcemia; blood ionized calcium concentrations should be measured since calcium depletion occurs secondary to citrate chelation; calcium replacement should be administered intravenously (see Table below)

	Calcium P	reparations ar	nd Their Use	
Solution	Elemental Calcium	Unit Volume	Total Elemental Calcium	Osmolarity
10% Calcium chloride	27 mg (1.36 mEq)/ml	10 ml Ampule	270 mg/10 ml	2,000 mOsm/l
10% Calcium gluconate	9 mg (0.46 mEq)/ml	10 ml Ampule	90 mg/10 ml	680 mOsm/l
10% Calcium chloride continu- ous infusion	2.45 mg/ml	5 Amps/ 500 ml NS	1,350 mg/550 ml	200 mOsm/l
10% Calcium gluconate contin- uous infusion	0.82 mg/ml	5 Amps/ 500 ml NS	450 mg/550 ml	67 mOsm/l

- Transfusion reaction (given cumulative risk of clerical errors)
- Hyperkalemia (secondary to hemolysis in stored blood)
- Transfusion-related immunomodulation (TRIM) increased risk for infection
- Transfusion-related acute lung injury (TRALI)
- Transfusion-associated circulatory overload (TACO)

Strategies to Reduce Complications associated with Massive Transfusion

• Massive transfusion protocols should be established with standardized policies to reduce complications related to transfusion therapy

Strategies t	to Reduce Transfusion-Related Complications
Complication	Strategies to Reduce Complication
Hypothermia	Warm the room Surface warm the patient with heating blankets, heating lamps Heat and humidify inspired gases for ventilators Warm all IV fluids and blood products administered
Coagulopathy	Transfuse RBC: FFP in 1:1 ratio Check coagulation testing, including fibrinogen Transfuse cryoprecipitate if fibrinogen concentration low
Thrombocytopenia	Transfuse platelets to keep platelet count >100,000 $(100 \times 109/I)$ to form stable clot
Electrolyte abnormalities	Measure blood potassium, calcium, and magnesium concentrations Replete electrolytes to normal values as indicated
Acid-base disorders	Sodium bicarbonate or tromethamine for severe metabolic acidosis with hemodynamic instability or renal failure
TRALI	Use restrictive transfusion strategy once hemorrhage controlled Use FFP from men or nulliparous women
TACO	Discontinue crystalloid fluid resuscitation Consider IV diuretic use

• Once definitive hemorrhage control has been achieved and the patient is hemodynamically stable, a restrictive approach to transfusion should be implemented, with RBC transfusion for hemoglobin <7 g/dl.

VENOUS THROMBOEMBOLISM AND PULMONARY EMBOLISM, PREVENTION STRATEGIES

- VTE includes both deep vein thrombosis (DVT) and pulmonary embolism (PE)
- Critically ill patients are at increased risk of developing VTE; untreated PE has a mortality rate of 25%.
- Risk factors that predispose ICU patients to VTE include factors common in the general medical population (cancer, surgery, trauma) as well as factors acquired in the ICU (e.g., sedation, immobility, mechanical ventilation, platelet transfusion, vasopressor use, dialysis-dependent renal failure).
- VTE risk increases with age.
- DVT complications include post-thrombotic syndrome, phlegmasia cerulean dolens (venous gangrene)
- Complications associated with ICU-acquired VTE increase morbidity, mortality length of stay, and costs.
- Without thromboprophylaxis, VTE incidence ranges from 15% to 60%.
- Systematic implementation of VTE prophylaxis significantly reduces this rate.
- All ICU patients should be evaluated on ICU admission for the appropriate VTE prophylaxis

therapy.

• The American College of Chest Physicians (ACCP) publishes guidelines for VTE prophylaxis in ICU.

ACCP Guideline Recommendations for Thromboprophylaxis in ICU Patients

- For patients admitted to a critical care unit, we recommend routine assessment for VTE risk and routine thromboprophylaxis in most (grade 1A).
- For critical care patients who are at moderate risk for VTE (e.g., medically ill or postoperative general surgery patients), we recommend using LMWH or UFH thromboprophylaxis (grade 1A).
- For critical care patients who are at higher risk (e.g., following major trauma or orthopedic surgery), we recommend LMWH thromboprophylaxis (grade 1A).
- For critical care patients who are at high risk for bleeding, we recommend the optimal use of mechanical thromboprophylaxis with graduated compression stockings and/or intermittent pneumatic compression at least until the bleeding risk decreases (grade 1A). When the high bleeding risk decreases, we recommend that pharmacologic thromboprophylaxis be substituted for or added to the mechanical thromboprophylaxis (grade 1C) (*Chest.* 2008;133(Suppl 6):381S).

Diagnostic tests for VTE and PE

- Venous duplex ultrasound of the 4 extremities is the best diagnostic test for VTE in ICU patients
- D-dimer assay has high sensitivity (98%) and modest specificity (50%) is useful for excluding DVT and PE, but not useful for confirming diagnosis. Should not be used in surgical, pregnant or cancer patients.
- In ICU patients with possible PE, computed tomographic pulmonary angiography (CTPA) is indicated.
- If normal CXR and contraindication to CTPA (1st trimester pregnancy, IV contrast allergy, impaired renal function) then V/Q scan is useful. If abnormal CXR, steroid/antihistamine pretreatment for IV contrast allergy. If severe allergy, weight risks and benefits of empiric therapy for VTE.
- Transthoracic echocardiography (TTE) findings of right ventricular strain or dysfunction may be suggestive of PE but are not diagnostic of PE, it may be helpful for ICU patients unable to travel to radiology (*N Engl J Med.* 2006;354(22):2317).

Treatment of VTE and PE

- Treatment of uncomplicated VTE is systemic anticoagulation with unfractionated heparin (UFH) or with low molecular weight heparin (LMWH) with subsequent warfarin for 6 mo duration.
- For patients with absolute contraindication to anticoagulation, inferior vena cava filter is indicated
- Patients with TTE findings consistent with massive PE or with significant cardiovascular compromise should receive either direct or systemic thrombolysis.
- Patients with cardiopulmonary arrest from suspected PE, consider immediate catheter thrombectomy, systemic or direct thrombolysis, extracorporeal membrane oxygenation (ECMO), or surgical thrombectomy.

Heparin-Induced Thrombocytopenia

- HIT is an anticoagulant-induced *prothrombotic* disorder
- HIT is an immune-mediated adverse drug effect characterized by platelet activation,

- hypercoagulability and increased risk of thrombosis, both venous and arterial.
- HIT is caused by platelet-activating heparin-dependent antibodies of immunoglobulin G class
- HIT should be considered when the platelet count falls to $<150 \times 10^9/l$ (or by >50% from baseline) between days 5 and 14 of exposure to any heparinoid product
- Rapid-onset HIT can occur if heparin is given to a patient who already has circulating HIT antibiotids, usually due to heparin given in the last 5–100 days.
- Thrombocytopenia in HIT is usually moderate mean platelet count $60 \times 10^9/l$
- Thrombocytopenia in HIT usually recovers within a few days of heparin discontinuation
- Reported mortality rate with HIT ranges between 10% and 20%
- A high index of suspicion is required for early recognition of HIT
- A clinical scoring system is used to identify patients with HIT, called the "4 Ts"

	Points (0, 1, or 2 for Each of the 4 Categories): Maximum Score = 8				
	2	1	0		
Thrombocytopenia	>50% platelet decrease to nadir ≥20	30–50% platelet decrease, or nadir 10–19, or >50% decrease secondary to surgery	<30% platelet decrease, or nadir <10		
Timing* of onset of platelet decrease (or other sequelae of HIT)	Days 5–10 or ≤day 1 with recent heparin (past 30 days)	>Day 10 or timing unclear; or <day 1<br="">with recent heparin (past 31–100 days)</day>	<day (no="" 4="" heparin)<="" recent="" td=""></day>		
Thrombosis or other sequelae	Proven new thrombosis, skin necrosis, or acute systemic reaction after Intravenous unfraction- ated heparin bolus	Progressive or recur- rent thrombosis, ery- thematous skin lesions, suspected thrombosis (not proven)	None		
Other causes of platelet decrease	None evident	Possible	Definite		

^{*}First day of immunizing heparin exposure considered day 0. Pretest probability score: 6–8 indicates high; 4–5, intermediate; and 0–3, low. Adapted from Warkentin TE: Heparin-induced thrombocytopenia: Diagnosis and management. Circulation 2004;110:e454–e458.

• Once HIT is strongly suspected in a critically ill patient, all of the following should occur:

Principles o	fTreatment for Suspected or Confirmed HIT: The "Six A's"
Two "Do's"	Avoid and discontinue all heparin (including low molecular weight heparin)
	 Administer an alternative non-heparin anticoagulant; recommend a direct thrombin inhibitor (DTI)
Two "Don'ts"	3. Await platelet recovery before initiation of warfarin anticoagulation
	4. Avoid platelet transfusions
Two Diagnostics	5. Anti-PF4/heparin antibody test for confirmation
	6. Assess for lower extremity deep venous thrombosis

			Non-Heparin Anticoagulants	for HIT Treatment		
Drug	Mechanism	Approved for HIT	Half-Life	Monitoring	Dosing	Clearance
Fondaparinux	long-acting AT3- dependent inhibition of factor Xa	Not approved for HIT treatment in U.S.	Long (24 hr); avoids potential for rebound hypercoagulable state	Direct (anti-Xa levels): accurate drug levels obtained	Not established for HIT, but consider 7.5 mg once daily (prophylaxis dose is 2.5 mg daily)	Renal
Danaparoid	long-acting AT3- dependent inhibition of factor Xa	Not approved for HIT, not available in U.S., Approved for HIT in Canada, Europe, Australia, New Zealand and Japan.	Long (17–20 hr) avoids potential for rebound hypercoagulable state	Direct (anti-Xa levels): accurate drug levels obtained	Bolus: 2,250 Ü IV only in life-or limb-threatening thrombosis; infusion, 400 U/h × 4 h, then 300 U/h × 4 h, then 200 U/h IV, subsequently adjusted by anti-Xa levels (target, 0.5–0.8 anti-Xa U/ml)	Renal
Argatroban	Direct thrombin inhibitor (DTI)	Approved for HIT treatment in U.S.	Short (40–50 min); potential for rebound hypercoagulable state	Indirect (APTT): risk for DTI underdosing due to APTT elevation for non-DTI factors	No bolus; initial rate, 0.5–2 mog/kg/min (adjust to APTT); Reduce in liver disease	Hepatobiliary
Lepirudin	Direct thromb in inhibitor (DTI)	Approved for HIT treatment in U.S.	Short (80 min); potential for rebound hypercoagulable state	Indirect (APTT): risk for DTI underdosing due to APTT elevation for non-DTI factors	No bolus; initial rate, 0.10 mg/kg/h (adjust to APTT); reduce dose for renal dysfunction	Renal
Bivalirudin	Direct thrombin inhibitor (DTI)	Not approved for HIT treatment in U.S.	Short (25 min); potential for rebound hypercoagulable state	Indirect (APTT):risk for DTI underdosing due to APTT elevation for non-DTI factors	Not established; no bolus; initial dose, 0.15–0.20 mg/kg/h has been suggested	Enzymic metabolism

APTT, activated partial thromboplastin time.

Above tableadapted from: Warrient in T.E.G. setracher A., Koster A., et al. Treatment and prevention of haparin-induced thrombocytopenia. American College of Chest Physicians evidence-based clinical practice guidelines (9th edition). Chest 2008;133 (Suppl 6):940S-80S

Disorder	Common Clinical Manifestations	Useful Clinical Laboratory Analyses	me or Disseminated Intravascular Coagulation. Comments
Heparin-induced thrombocytopenia (HIT)	:50% present with thrombosis; venous thrombosis > arterial	Anti-heparin/PF4 antibody testing (ELISA, functional assays).	Temporal relationship with heparin or LMWH therapy.
Antiphospholipid syndrome (APS)	Recurrent venous and/or arterial thromboembolic complications; recurrent fetal loss.	Anticardiolipin antibody and anti-52- glycoprotein 1 antibody testing (ELISA); lupus anticoagulant testing.	Autoimmune disorder, either primary or associated with other rheumatologic conditions (eg, lupus); in some cases, may be drug-induced (eg, procainamide).
Disseminated intravascular congulation (DIC)	Hemorrhagic or thromboembolic events pre- dominate, depending on underlying cause and dinical course.	PT, PTT, thrombin time, fibrinogen, D-dimer.	May be acute (eg. associated with sepsis, obstetric compli- cations, severe trauma) or chronic (eg. associated with cancer, sortic aneurysm), DIC can complicate severe HIT
Thrombotic thrombocytopenic purpura (TTP)	Neurologic manifestations may include stroke, TIA, altered mental status, seizures; other symptoms include fever, renal insufficiency.	Microangiopathic hemolytic changes on blood film, elevated LDH, decreased ADAMTSI 3 levels.	Associated with severe ADAMTS13 deficiency due to inhibitors in most patients; may be seen in patients taking ticlopidine or dopidogrel, or with other drugs, (eg. cyclosporine, tarrolimus, mitomycin). Microangiopathy can also be seen in severe HIT with associated DiC.
Drug-induced thrombo cytopenia (non-heparin)	Petechiae, purpura, and other hemorrhagic symptoms with severe thrombocytopenia.	Isolated thrombo cytopenia, may be severe.	Associated with multiple drugs (eg, abciximab, quinine, multiple antibiotics).
Post-transfusion purpura (PTP)	Hematoma, ecchymoses, pur pura.	Severe thrombocytopenia that begins approximately five days after blood prod- uct use.	Temporal relationship to transfusion therapy; most com- mon in multiparous females. The timing of PTP approxi- mately one week after surgery can mimic HIT.

UNWH includes low molecular weight heparin, D.C., deseminated in travascular congulation; B.SA, enzyme-linked immunosorbant assay, T.A., tensient ischemic attack, PT, prothrombin time; PTT, partial thrombospondin components 13.

From: Ontal TL. Heparin-Induced thrombocycopenis: When a low platelet count is a manchine for anticoagulation He motobyy Am Soc Hemato I Educ Program, 2009;225–232.

- Do not wait for laboratory confirmation of HIT prior to initiation of a DTI this is associated with increased risk for thrombosis and adverse outcome.
- HIT diagnosis is confirmed with either a positive anti-PF4/polyanion-IgG enzyme immunoassay (EIA) or a positive platelet activation assay (i.e., serotonin-release assay, SRA)
- Once platelet count has normalized, warfarin should be initiated with a low maintenance dose (specifically, no loading dose) and overlapped with the non-heparin anticoagulant until the target international normalized ratio (INR) has been reached and for a minimum of 5 days
- The duration of warfarin therapy should be standard for venous thromboembolism (VTE), for a minimum of 3 mos with consideration for a more extended course depending on clinical circumstances related to the thromboembolic event. (*Crit Care Med.* 2006;34:2898)

Hypercoagulable States and Coagulopathies Hypercoagulable States

- Hypercoagulable states should be considered in ICU patients who develop venous or arterial thrombosis
- Hypercoagulable states can be inherited or acquired
- Acquired thrombophilia is related to risk factors or predisposing conditions for thrombosis, including surgery, trauma, malignancy, central venous catheter, use of oral contraceptives, and others.
- Inherited thrombophilia is a genetic tendency to VTE

- Factor V Leiden is the most common cause of inherited thrombophilia, accounting for 40%–50% of cases
- The prothrombin 20210A gene mutation, and deficiencies in protein S, protein C, or antithrombin account for most of the remaining cases of inherited thrombophilia.

Diagnostic Testing for Hypercoagulable States

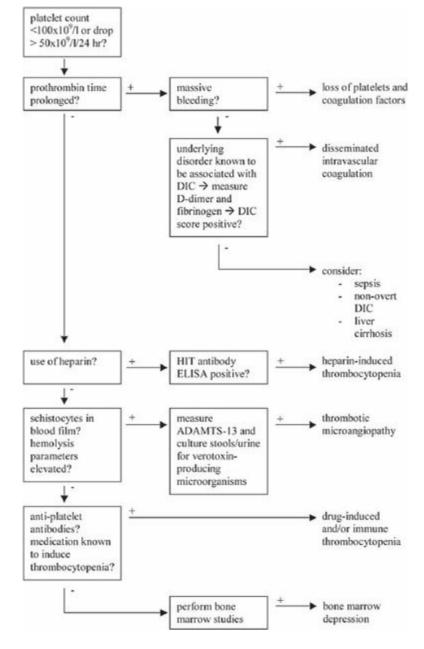
- Complete blood count
- Activated Protein C (APC) resistance test
- Prothrombin 20210A mutation
- Antithrombin III Activity
- Protein C Activity
- Protein S Activity
- ELISA anti-PF4 antibody (for HIT diagnosis)
- Cardiolipin Antibody (IgG and IgM)
- β₂-glycoprotein-1 Antibody (IgG and IgM)
- Lupus Anticoagulant
- Homocysteine levels
- Factor VIII Activity
- Fibrinogen (Clottable)
- Fibrinogen Antigen
- Plasminogen Activity
- Hexagonal Phospholipid Neut
- Dilute Russel's Viper Venom
- Aspirin and/or Plavix resistance (VerifyNow rapid assay)

Treatment of Hypercoagulable States

- Initial treatment of venous or arterial thrombosis in an ICU patient is systemic anticoagulation.
- Antithrombin, protein C, or protein S deficiency carries VTE recurrence rates of 5%–15% per year, a relative increase of 2.5 compared with rates in the absence of thrombophilia
- Patients heterozygous for factor V Leiden or the prothrombin G20210A mutation are much less prone to VTE recurrence with a relative risk of 1.3 to 1.4; VTE recurrence rates are 5-fold greater with homozygosity or double heterozygosity.
- A mild/moderate increase in homocystein level is associated with a 2.5 increased risk for recurrent VTE
- Long-term anticoagulant therapy is recommended in selected high-risk hypercoagulable states after a 1st spontaneous VTE episode in antithrombin, protein C or protein S deficiency, and for patients homozygous or doubly heterozygous for factor V Leiden and/or the prothrombin mutation.
- For patients with lower risk for recurrence, they are treated with anticoagulation for 6 mos, and then imaging for residual thrombosis or D-dimer testing are performed at the end of anticoagulant therapy, and the results are used to determine likelihood of VTE recurrence.

Coagulopathies

Differential Diagnostic Algorithm for Coagulation Abnormalities in the Intensive Care Unit



DIC, disseminated intravascular coagulation; ELISA, enzyme-linked immunosorbent assay; HIT, heparin-induced thrombocytopenia.

From: Levi M, Opal SM. Coagulation abnormalities in critically ill patients. Crit Care. 2006;10(4):222.

- ICU patients with coagulation defects have a 4- to 5-fold increased risk for bleeding compared to patients with a normal coagulation status
- Disseminated intravascular coagulation (DIC) is a syndrome caused by systemic intravascular activation of coagulation with formation of microvascular thrombi with clotting factor consumption, and occurs in patients with infection, malignancy, trauma, amniotic fluid embolism and others.
- DIC manifests as prolonged plasma clotting times, thrombocytopenia, reduced plasma fibrinogen concentration, raised plasma fibrin-degradation products, and sometimes microangiopathic hemolysis.
- The most frequent cause of DIC is sepsis, with reduced protein C concentrations resulting in decreased endogenous fibrinolysis.
- ICU patients with severe sepsis or septic shock may manifest abnormalities in coagulation testing, but plasma should not be transfused unless the patient has evidence of clinical bleeding (Surviving Sepsis Guidelines 2008).
- Patients with sepsis-induced DIC may progress to purpura fulminans, a rapidly progressive

thrombotic disorder with hemorrhagic infarction of the skin and dermal vascular thrombosis.

- Protein C concentrations should be measured in patients with purpura fulminans.
- In patients with severe limb-threatening purpura fulminans and low protein C levels, replacement with exogenous protein C should be considered.
- Meningococcal and Pneumococcal sepsis are common causes of purpura fulminans and DIC.
- Treatment of DIC is supportive with aggressive treatment of the underlying cause of the DIC.
- Treatment of bleeding in DIC requires blood component replacement therapy with plasma, platelets and cryoprecipitate.

Hemostatic Resuscitation for Acute Traumatic Coagulopathy

- Hemorrhage is a major cause of trauma deaths and coagulopathy exacerbates hemorrhage
- Trauma patients with severe hemorrhage have early fibrinolysis in addition to coagulopathy
- Uncontrolled hemorrhage in trauma leads to the lethal triad of Acidosis, Hypothermia and Coagulopathy
- Prompt reversal of coagulopathy using "hemostatic resuscitation" with early use of blood component therapy is advocated as the optimal practice for patients requiring massive transfusion.
- Most severely injured patients are coagulopathic at hospital admission, before resuscitation interventions.
- An emerging consensus for hemostatic resuscitation in patients requiring massive transfusion is as follows:
 - Expedite the control of hemorrhage to prevent consumptive coagulopathy and thrombocytopenia and reduce the need for blood products;
 - Limit isotonic crystalloid infusion to prevent dilutional coagulopathy and thrombocytopenia;
 - Hypotensive resuscitation (SBP, 80–100 mm Hg) until definitive hemorrhage control is established;
 - Transfuse blood products in a 1:1:1 ratio of RBCs/FFP/platelets (one five-pack of pooled platelets counted as 5 units); and
 - Frequent laboratory monitoring (arterial lactate to assess adequacy of resuscitation, ionized calcium, and electrolytes).
- It is recognized that increased early use of plasma is associated with increased risk for acute lung injury (ALI-TRALI) and acute respiratory distress syndrome (ARDS), but is associated with decreased mortality.

ELECTROLYTES

Sodium and Total Body Water

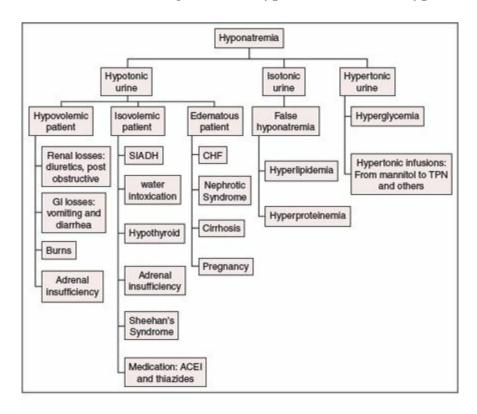
Sodium and total body water are intimately related issues. Clinical assessment of patients with hypernatremia or hyponatremia should include an assessment of their total volume status.

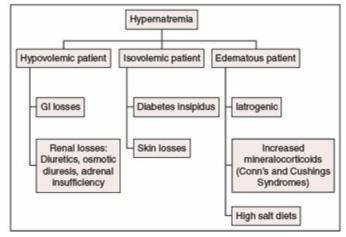
For details on hyponatremia and hypernatremia and their workup see Chapter 11.

Dec distr	Annual technological and desperation of the second	nostatic Testing Found \				and the second s	T-1000
Condition	PT	aPTT	Fibrinogen	FDP	Platelets	BT	TT
UPH	Normal or prolonged	Prolonged	Normal	Normal	Normal	Normal	Prolonged
LMWHs	Normal or prolonged	Normal or minimally prolonged	Normal	Normal	Normal	Normal	Normal or minimally prolonged
Direct factor Xa inhibitors	Normal or prolonged	Normal or minimally prolonged	Normal	Normal	Normal	Normal	Normal
Direct thrombin inhibitors	Prolonged	Prolonged	Normal	Normal	Normal	Normal	Prolonged
Coumadin	Prolonged	Normal or prolonged ^b	Normal	Normal	Normal	Normal	Normal
Vitamin K deficiency	Prolonged	Prolonged	Normal	Normal	Normal	Normal	Normal
Hepatic Insufficiency	Prolonged	Normal or prolonged	Low or normal	Normal or elevated	Low	Normal or prolonged	Prolonged
DIC	Normal or prolonged	Normal or prolonged	Normal or low	Elevated	Low	Prolonged	Prolonged
Dilution	Prolonged	Prolonged	Low ot normal	Normal	Low	Normal or prolonged	Normal or prolonged
von Willebrand Disease	Normal	Prolonged	Normal	Normal	Normal	Prolonged	Normal
Lupus anticoagulant	Normal or prolonged	Prolonged	Normal	Normal	Normal	Normal	Normal
Thrombocytopenia	Normal	Normal	Normal	Normal	Low	Normal or prolonged	Normal

BT, bleeding time, DIC, deseminated intravascular coagulation; FD gibrin degradation product; DTWH, low-molecular-weight heparin; TT, thrombin time; UFH, unfractionated heparin. See Table on p. 7 for expansion of other abbreviations.

Figure 4. Differential Diagnosis of Hyponatremia and Hypernatremia





^{*}At superheapositic desages.
*Early in cournadin treatment.
From: Wheeler AP, Rice TW Congulopathy in critically if patents: Part 2-colubb chating factors and he most at the testing. Chest. 2010 Jun; 137 (1):185–194.

Hypokalemia – Etiology

- Inadequate intake (<40 mEq/d)
- Increased excretion
 - Diarrhea, laxative abuse
 - Renal losses
 - Loop, thiazide diuretics
 - Metabolic alkalosis (vomiting, nasogastric drainage)
 - Osmotic diuresis (uncontrolled diabetes)
 - Non-reabsorbable anions (penicillin)
 - Magnesium depletion
 - Renal tubular acidosis (types 1 and 2)
 - Mineralocorticoid excess (i.e., primary hyperaldosteronism)
- Congenital adrenal hyperplasia (i.e., Liddle's, Gitelman's, Bartter's syndromes)
 - Intracellular shifts
 - metabolic alkalosis
 - Drugs
 - β-Adrenergic agonists
 - Bronchodilators, decongestants, tocolytic agents, theophylline, caffeine
 - Insulin
 - Delirium tremens
 - Hyperthyroidism
 - Familial hypokalemic periodic paralysis
 - Barium poisoning

Hypokalemia – *Clinical Significance*: Hypokalemia is well tolerated in otherwise normal individuals; it is associated with an increased incidence of life-threatening cardiac arrhythmias in patients with cardiac disease. Severe hypokalemia <2.5 mEq/l can cause rhabdomyolysis and, when the value is less than 2.0 mEq/l it can cause an ascending paralysis with eventual respiratory arrest.

Hypokalemia – EKG Findings: flattened T-wave, prominent U-wave.

Hypokalemia – *Treatment:* Diagnosis and treatment of the underlying cause is essential; Repletion under EKG monitoring in situations where intracellular potassium shifts are not in play; Intense repletion is dangerous and should be avoided.

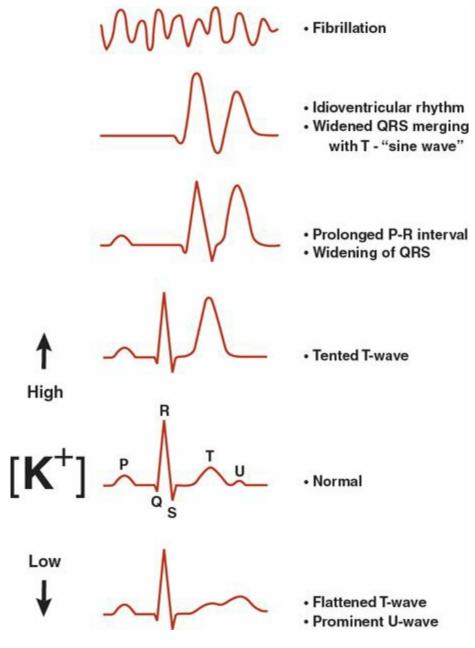
Hyperkalemia – Etiology

- Factitious
 - Thrombocytosis (platelets >1,000,000/mm³)
 - Leukocytosis (WBC >100,000/mm³)
 - Hemolysis
 - Repeated fist clenching with tourniquet in place
- Impaired K+ excretion
 - Renal insufficiency or failure
 - Mineralocorticoid deficiency
 - Addison's disease
 - Hyporenin hypoaldosteronism (type 4 renal tubular acidosis)

- Heparin-induced inhibition of aldosterone synthesis
- Hereditary enzyme deficiencies
- Pseudohypoaldosteronism
- Drugs
 - K+ -sparing diuretics (Spironolactone, amiloride, and triamterene)
 - ACE inhibitors
 - Angiotensin receptor blockers, NSAIDs, beta blockers, digoxin, heparin (see above), succinylcholine, cyclosporine, tacrolimus, trimethaprime, pentamidine
- Transcellular shifts
 - Metabolic or respiratory acidosis
 - Familial hyperkalemic periodic paralysis
- Release into the blood stream
 - Rhabdomyolysis
 - Burns
 - Trauma
 - Thrombocytosis
 - Hemolysis
 - Extremely high white cell counts.
- Iatrogenic: excessive replacement is a very frequent cause of hyperkalemia

Hyperkalemia – *Clinical Significance*: Hyperkalemia is asymptomatic, but impairs normal cardiac conduction, ECG changes: peaked T waves, widening of QRS (sinusoidal wave forms), can progress to asystole or ventricular fibrillation.

Figure 5. ECG Changes Due to Hyper- and Hypokalemia



Treatments for Hy	perkalemia	
Emergency	Response Time	Duration
Cardiac conduction abnormal Calcium gluconate or chloride ^a (10 ml of 10% solution)	Immediate	15–30 min
Serum [K ⁺] > 6.5 mEq/l or rising Glucose (50 ml of 50% solution) plus regular insulin 10 U	10–20 min	2–3 h
Albuterol 10–20 mg by inhaler over 10 min NaHCO ₃ ⁻ , only if metabolic acidosis present Kayexalate 15–30 g with sorbitol	20–30 min Delayed	2–3 h
By mouth	4–6 h	_
As retention enema	1 h	-
Loop diuretic (intravenous)	1 h	3 S
Hemodialysis	15-30 min	

^{*}Intravenous calcium should not be given in the setting of digoxin toxicity.

Hyperkalemia – *Treatment:* Regardless of the cause, therapy to lower serum potassium should be initiated immediately if the concentrations are greater than 5.5 mEq/l or if the ECG shows signs of conduction abnormalities.

• Strategies for the management of hyperkalemia (for the specific interventions and their mode of

action see table below):

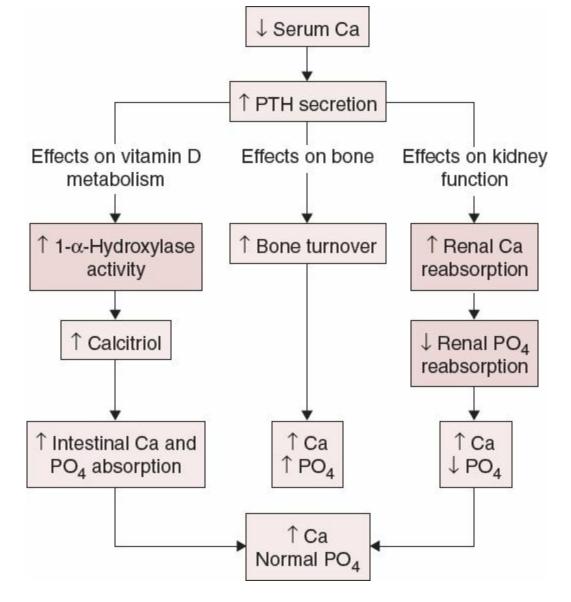
- I. Stabilize membranes (calcium)
- II. Drive K back into cells (insulin, bicarbonate, b-agonists)
- III. Decrease total body K (sodium polystyrene, loop diuretics, hemodialysis)
- Interventions effective for the treatment of hyperkalemia:

Mechanism	isms of Intervention	Dose	Onset	Comments	
Stabilize Membranes	Calcium Gluconate Calcium Chloride	1–2 amps IV	<5 min	Transient effect	
Drive potas- sium into cells	Insulin	Regular insulin 10 units IV with 1–2 amps of D50		Especially when hyperglycemia related	
	Bicarbonate	1-3 amps IV	15-30 min		
	β-2 Agonists	Albuterol 10-20 mg inhaled	30–90 min		
Remove potassium	Cation Exchange Resin	Sodium polystyrene (Kayexalate) 30–90 g PO or PR	1–2 hr	Risk of intestinal necrosis with sor- bitol formulation	
	Diuretics	Furosemide 40 mg IV or more	30 min	Unclear utility in short-term	
	Renal Replacement Therapy	Hemodialysis			

Adapted from Sabatine M., Pocket Medicine 2nd ed.

Calcium

Figure 6. Effects of Hypocalcemia on Calcium and Phosphate Homeostasis



Hypercalcemia: total calcium >10 mg/dl and ionized calcium >1.3 mmol/l. *Hypercalcemia – Clinical Manifestations*

- Depends on the magnitude of hypercalcemia and the rate of rise in serum calcium.
- Gastrointestinal symptoms: nausea, vomiting, constipation, and abdominal pain.
- Neurologic symptoms: difficulty concentrating, fatigue, lethargy, and muscle weakness.
- Renal Symptoms: Nephrogenic diabetes insipidus and renal failure with volume depletion.
- Cardiovascular symptoms: hypertension and shortening of the QT interval. Severe arrhythmias are rare

Hypercalcemia – Etiology

- Malignancy
 - Local osteolytic hypercalcemia
 - Humoral hypercalcemia of malignancy (PTH-related peptide)
 - Hematologic malignancies (ectopic calcitriol synthesis)
- Hyperparathyroidism, thyrotoxicosis, pheochromocytoma, granulomatous diseases
- Drug-induced
 - Vitamin D
 - Thiazide diuretics
 - Estrogens and antiestrogens
 - Androgens (breast cancer therapy)

- Vitamin A
- Lithium
- Immobilization
- Total parentheraly nutrition
- Milk-alkali syndrome
- Kidney disease (acute and chronic, usually from medications)

Hypercalcemia – Treatment (Makras and Papapoulos 2009)

- **General Measures**: volume repletion with saline to counteract the kidney's increase of its tubular reabsorption of sodium to maintain normovolemia. This is associated with increased tubular reabsorption of calcium.
- Diuretics: Loop diuretics, particularly furosemide because they increase urinary calcium excretion.
- **Bisphosphonates**: Currently the treatment of choice for malignancy associated hypercalcemia due to their inhibitory action on bone resorption. (zoledronate, pamidronate)
- **Steroids**: Glucocorticoids have been used in the past to treat hypercalcemia, especially in patients with hematologic malignancies. Today their use is restricted to the treatment of hypercalcemia due to ectopic production of 1,25(OH)₂D.
- Hemodialysis

Hypocalcemia: total calcium < 8.6 mg/dl and ionized calcium < 1.12 mmol/l.

Hypocalcemia - Clinical Manifestations

- Depends on the magnitude of hypocalcemia and the rate of fall in serum calcium.
- Neurologic symptoms: perioral numbness and carpopedal spasms of the hands and feet. In some patients these spasms may progress to tetany.
- Chvostek's and Trousseau's signs. Chovostek's sign is tested by tapping on the facial nerve near the temporal mandibular joint and watching for grimacing caused by spasm of the facial muscles. Trousseau's sign is tested by inflating a blood pressure cuff above the systolic blood pressure for 3 min and watching for spasm of the outstretched hand.

Hypocalcemia – Etiology

- Hypoalbuminemia has to be ruled out
- Vitamin D deficiency
- Hypoparathyroidism
- Pseudohypoparathyroidism (hypocalcemia and hypophosphatemia but elevated PTH, indicating non-responsiveness to PTH)
- Tissue consumption of calcium:
 - Precipitation into, as in pancreatitis.
 - Excess bone formation in some malignancies with blastic bone metastases
 - Following parathyroidectomy
- Hypomagnesemia
- Following acute hyperphosphatemia caused by rhabdomyolysis or tumor lysis syndrome, the phosphorus binds to calcium, leading to a drop in ionized calcium.
- Citrate infusion for renal replacement therapy or with blood and plasma transfusions
- Sepsis (unclear mechanism)

Hypocalcemia – Treatment

• IV calcium infusions are indicated only in the setting of symptomatic hypocalcemia and should not

be given in the presence of hyperphosphatemia because of the risk of precipitation.

- Asymptomatic patients should be repleated with oral calcium. The amount of calcium absorbed will be increased if calcitriol is given with the calcium.
- Hypomagnesemia should be treated concomitantly.
- If appropriate, patients may be changed from loop diuretics to thiazides
- Treatment of the underlying disease

Magnesium

Hypermagnesemia

- Rare diagnosis because of the kidney's high clearance of magnesium
- Symptoms: lethargy and confusion, arrhythmias, and muscle weakness. (pregnant patients treated with magnesium with serum levels of 4 to 6 mg/dl are usually asymptomatic)
- Etiology: increased intake, decreased renal function, or lithium toxicity.
- Treatment: stopping the magnesium intake and adequate volume repletion.

Hypomagnesemia

- Common in both hospitalized and ICU patients
- Symptoms: apathy, depression, delirium, seizures and paresthesias, tremors, general muscle weakness, ventricular arrhythmias, and increased susceptibility to Digoxin-related arrhythmias. Commonly is associated with other electrolyte abnormalities, including hypokalemia, hyponatremia, hypocalcemia, and hypophosphatemia.
- Etiology
 - Reduced intake: starvation, alcoholism, prolonged postoperative state
 - Redistribution from extracellular to intracellular: insulin, parathyroidectomy, Catecholamine excess states, acute pancreatitis, excessive lactation
 - Reduced absorption: specific or generalized malabsorption syndrome, extensive bowel resections, chronic diarrhea, laxative abuse,
 - Drug-induced losses: diuretics, aminoglycosides, digoxin, cisplatinum, and cyclosporine
 - Hormone-induced magnesuria: aldosteronism, hypoparathyroidism, hyperthyroidism
 - Renal losses due to polyuria: hypercalcemia, hyperglycemia extracellular fluid volume expansion.
 - Phosphate depletion syndrome, alcohol ingestion
- Treatment: hypomagnesemia should be treated with IV or oral supplementation

Phosphate

Hyperphosphatemia

- Common causes include renal failure (decreased phosphate excretion), increased extracellular phosphate causes (tumor lysis syndrome, rhabdomyolysis, hemolysis), and increased phosphate reabsorption (hypoparathyroidism, acromegaly, treatment with bisphosphonates, or vitamin D).
- Treatment for chronic condition: low phosphate diet and phosphate binders
- Treatment for acute condition: saline infusion to increase phosphate excretion, hemodialysis

Hypophosphatemia

- Common causes include chronic alcoholism, malnutrition, TPN with inadequate phosphate, and chronic ingestion of antacids. Monitor for refeeding syndrome in patients with malnutrition.
- Signs include myopathy, ileus, rhabdomyolysis, respiratory failure, cardiac failure, metabolic encephalopathy, confusion, seizures, delirium, and coma.
- If IV therapy is necessary in the symptomatic patient, the dose depends on the severity of

hypophosphatemia. For moderate hypophosphatemia (i.e., levels between 1.25 to 2.5 mg/dl), 0.08 to 0.24 mmol/kg (maximum total dose of 30 mmol) may be given over 6 hr. for more severe hypophosphatemia, 0.25–0.5 mmol/kg (maximum total dose of 80 mmol) may be given over 8–12 hr

FLUID RESUSCITATION AND IV REPLACEMENT SOLUTIONS

Crystalloids

- Fluid resuscitation with isotonic crystalloid solutions (lactated ringer's, normal saline) is recommended in ICU patients with hypovolemic, hemorrhagic, or distributive shock.
- Albumin resuscitation is only indicated for patients with liver disease/ascites and nephrotic syndrome
- The Saline vs. Albumin Fluid Evaluation (SAFE) study demonstrated that in ICU patients, use of either 4% albumin or normal saline for fluid resuscitation resulted in similar 28-day mortality rates, outcomes (*N Engl J Med.* 350(22):2247).
- A follow-up study to the SAFE trial reported that albumin was associated with higher mortality rates in traumatic brain injury (TBI) patients.
- Hypertonic saline is considered in severe TBI and intracranial hypertension.
- Pre-hospital hypertonic saline or hypertonic saline/dextran compared with normal saline for severe TBI patients not in hypovolemic shock did not improve their 6-mo neurologic outcome or survival (*JAMA*. 2010 Oct 6;304(13):1455–1464).
- In patients with severe sepsis randomized to 10% pentastarch, a low-molecular-weight hydroxyethyl starch (HES 200/0.5), or Ringer's lactate for fluid resuscitation, HES was harmful with higher rates of acute renal failure and renal replacement therapy, and its toxicity increased with accumulating doses (N Engl J Med. 358(2):125).

		The Compositi	ion of Crystalloid and	Colloid Resustitation	Fluids		
	La ctated Ringer's (LR)	Normal saline (0.9 NS)	Half normal saline (0.45 NS)	DSW	3% NaCI	Albumin 5%	Hetastarch 6%
Sodium (Na+)	130 mmol/1	154 mmol/1	77 mmol/l	-	513	150	154
Chloride (CT)	109 mmol/I	154 mmol/1	77 mmol/l	-	513	150	154
Potassium (K+)	4 mmol/l	-	14	-	12	-	-
Calcium (Ca++)	3 mmol/l	-	12	-	2	-	
Lactate	28 mmol/l	-	2		12	-	_
Glucose	-	-	7	50 g; 2.78 mmol/l	<u></u>	-	70
pН	6.5	5.0	5.0	4.0	72		-
Osmolality	275 mosm/l	308 mosm/1	-	-	1,025 mosm/l	310 mosm/l	310 mas m/l
Tonicity	Isotonic	Isotonic	Hypotonic	Hypotonic	Hypertonic	2010/2010/2010	
Cost	\$1.26	\$1.44	\$126	\$1.26	\$1.28	\$100	\$27.30
Comments	Ruid choice for initial resuscitation	Alternative to LR; watch for Hypernatremia, Hyperchloremic acidosis	Common mainte- nance fluid, with or without dextrose	Ruid choice in hyper- natremia.Watch for hyponatremia	Risk of hyper-natre- mis; consider in patients un-respon- sive to isotonic fluid	Indicated only in liver disease and nephrotic syndrome	No specific indication in ICU patients for fluid resuscitation; potential harm in sepsis

ACID-BASE MANAGEMENT

MARY B. RICE, MD • KATHRYN A. HIBBERT, MD • ATUL MALHOTRA, MD

Definitions

- Acidemia pH < 7.36, alkalemia pH > 7.44
- pH is determined by P_aCO₂ and HCO₃⁻
 - Henderson equation: $H^+ = 24 \times P_a CO_2/HCO_3^-$
 - Normal H⁺ = 40 nM, $P_aCO_2 = 40$ mm Hg and $HCO_3^- = 24$ meq, 40 = 40 for internal consistency
 - Carbonic acid equilibrium:

$$H_2O + CO_2 \longleftrightarrow H_2CO_3 \longleftrightarrow H^+ + HCO_3^-$$

- Lungs regulate P_aCO₂ and kidneys regulate HCO₃⁻ to control pH
- Acidemia vs. acidosis
 - Acidemia: low blood pH
 - Acidosis: a disturbance causing proton production

Workup

- \sqrt{pH} , P_aCO_2 , electrolytes, albumin to identify primary disorder
- Assess if disorder is simple or mixed by checking if the response is as expected
- If HCO_3^- (in respiratory disorder) or P_aCO_2 (in metabolic disorder) is not the expected value, there is >1 primary acid—base disorder
- Pneumonic for the expected response of the lungs/kidneys to primary disturbance: "1 for 1, 10 for 7, 1, 4, 2, 5"
 - Numbers represent expected response in alphabetical order: Metabolic before Respiratory, Acidosis before Alkalosis, Acute before Chronic

	Primary Acid	l-Base Disturbances	
Primary Disorder	Recommended Pneumonic	Other Formulas to Predict Response	Example
Metabolic Acidosis	"1 for 1" Every $1 \downarrow$ in $HCO_3^- \rightarrow 1 \downarrow P_aCO_2$	$P_aCO_2 = 1.5 \times HCO_3^-$ + 8 (+/-2) (Winter's Formula) $P_aCO_2 = last 2 digits$ of pH	pH = 7.30 P_aCO_2 = 31, HCO_3^- = 15 → HCO_3^- ↓ by 9, P_aCO_2 ↓ by 9
Metabolic Alkalosis	"10 for 7" Every 10 ↑ in HCO ₃ ¬ → 7 ↑ P _a CO ₂	P _a CO ₂ = 0.9 × HCO ₃ ⁻ + 16	pH = 7.47, P_aCO_2 = 47, HCO_3^- = 34 $\rightarrow HCO_3^- \uparrow$ by 10, $P_aCO_2 \uparrow$ by 7
Acute Respiratory Acidosis	"1" Every $10 \uparrow P_aCO_2 \rightarrow 1 \uparrow HCO_3^-$	Every 10 \uparrow P _a CO ₂ \rightarrow 0.08 \downarrow pH	pH = 7.25, P_aCO_2 = 60, HCO ₃ ⁻ 26 → $P_aCO_2 \uparrow$ by 20, HCO ₃ ⁻ ↑ by 2
Chronic Respiratory Acidosis	"4" Every $10 \uparrow P_aCO_2 \rightarrow 4 \uparrow HCO_3^-$	Every 10 \uparrow P _a CO ₂ \rightarrow 0.03 \downarrow pH	pH = 7.35, P_aCO_2 = 60, HCO_3^- = 32 → $P_aCO_2 \uparrow$ by 20, $HCO_3^- \uparrow$ by 8
Acute Respiratory Alkalosis	"2" Every $10 \downarrow P_aCO_2 \rightarrow 2 \downarrow HCO_3^-$	Every 10 \downarrow P _a CO ₂ \rightarrow 0.08 \uparrow pH*	pH 7.62, P_aCO_2 20, HCO ₃ ⁻ 20 \rightarrow $P_aCO_2 \downarrow$ by 20, HCO ₃ ⁻ \downarrow by 4
Chronic Respiratory Alkalosis	"5" Every $10 \downarrow P_aCO_2 \rightarrow 5 \downarrow HCO_3^-$	Every 10 ↓ P _a CO ₂ → 0.03 ↑ pH*	pH = 7.45, P_aCO_2 = 25, HCO ₃ ⁻ = 17 → $P_aCO_2 \downarrow$ by 15, HCO ₃ ⁻ \downarrow by ~8

^{*}pH changes are less predictable in respiratory alkalosis compared to acidosis.

- "Strong ion difference" = an alternative approach to acid—base chemistry based on conservation of mass and electrochemical neutrality. pH determined by:
 - Strong ion difference = $Na^+ + K^+ + Ca + Mg^{2+} Cl^- lactate$
 - Concentration of weak acids (proteins and phosphates)
 - P_aCO_2
- Stewart (strong ion) hypothesis is less practical for bedside acid—base analysis because it requires complex calculations but is conceptually useful

Management of Severe Acid-Base Disturbances in Critical Illness Systemic Effects of Acidemia

- CV: ↓ CO, arterial dilation (hypotension), venoconstriction, reentrant arrhythmias, ↓ Threshold for VF, ↓ Response to catecholamines/pressors
- Resp: resp muscle fatigue, dyspnea
- Metabolic: ↑ metabolic demands, inhibition of anaerobic glycolysis, ↓ ATP synthesis, ↑ K⁺, insulin resistance
- Cerebral: inhibition of cell volume regulation → coma

Treatment of Severe Acidemia (NEJM. 1998;338(1):26–34)

- Treat underlying cause
- IV NaHCO₃ until pH \geq 7.2 and HCO₃⁻ reaches 8–10 mmol/l
- Assume HCO_3^- space of 50% body weight, e.g., to $\uparrow HCO_3^-$ from 4 to 8 mmol/l in 70 kg patient give 140 mmol HCO_3^- (4 mmol/l \times 50% \times 70 kg)

- Infuse NaHCO₃ in isotonic solution (e.g., 3 amps NaHCO₃ in D5W, 150 mmol HCO₃⁻/l) over minhrs (bolus occasionally effective but no longer ACLS recommended)
- If intubated, consider increasing minute ventilation
- Oral therapy not reliable in critical illness
- HD can rapidly correct acidemia
- Problems encountered in treatment of acidemia
 - "Overshoot" alkalosis, esp. if underlying condition (e.g., DKA) resolves
 - Buffering of H⁺ by HCO_3^- causes \uparrow PCO_2 in cells. If no pulmonary reserve or undergoing CPR, paradoxical intracellular or even extracellular acidosis may occur if \uparrow $PCO_2 >> \uparrow$ HCO_3^-

Systemic Effects of Alkalemia

- CV: arteriolar constriction (esp. resp alkalosis), angina, \(\subseteq \text{SVT}, \(\subseteq \text{VT/VF} \)
- Resp: ↓ ventilation → hypoxemia, reversal of hypoxic pulmonary vasoconstriction → worse V/Q matching
- Metabolic: anaerobic glycolysis, \uparrow lactate, ketones $\rightarrow \uparrow$ AG, \downarrow K⁺, iCa²⁺, Mg²⁺, Phos
- Cerebral: ↓ cerebral blood flow, cerebral vasoconstriction, tetany, seizure, lethargy, delirium, stupor

Treatment of Severe Alkalemia (*NEJM*. 1998;338(2):107–111, *NEJM*. 2002;346(1):43–53)

- Treat underlying cause: antiemetics for N/V, H2 blockers if NGT suction required, ↓ loop/thiazide diuresis, add K⁺-sparing diuretic or acetazolamide, IVF if vol depleted (e.g., NS + KCl)
- Correct until $HCO_3^- < 40 \text{ mmol/l } (\sim pH < 7.55)$
- Severe alkalemia is usually chloride-responsive. Correcting Na⁺, Cl[−], K⁺ deficits often → bicarbonaturia
- IV HCl if rapid correction needed: 100–200 mmol (0.1–0.2 N) HCl/l D5W via central line, max rate 0.2 mmol/kg/hr
- Arginine HCl and NH₄Cl are occasionally used but reports of hyperkalemia and encephalopathy
- HD can rapidly correct alkalemia
- If saline-resistant alkalemia (i.e., mineralocorticoid excess), aggressively replete KCl
- Fluid overload is a common complication of alkalemia treatment (especially in cardiac/ renal failure)

METABOLIC ACIDOSIS

Approach to Metabolic Acidosis

Figure 1. Differential Diagnosis of Acidosis

Assess for presence of anion gap Anion gap = $Na - (CI + HCO_3^-)$ Normal AG is 8-12, but gap falls by 2.5 for every 1 fall in albumin AG Metabolic Acidosis Non-AG Metabolic Acidosis +AG = unmeasured anions (e.g., ketones, Due to bicarbonate loss or problem phosphates, sulfates, lactate) with renal NH₄⁺ production/excretion Find Source of AG Check Urine Anion Gap √ Serum Cr/BUN for uremia $UAG = U_{Na} + U_{K} - U_{CI}$ -Normally (-) due renal production √ Urine for ketones (acetoacetate) or serum beta-hydroxybutyrate of NH₄⁺ (unmeasured cation is urine) √ Lactic acid (-) UAG: kidneys appropriately √ Toxin screen excreting NH₄⁺ in response to √ Serum osm and calculate osmolar gap metabolic acidosis (e.g., diarrhea) (+) UAG: suggests renal cause OG = measured osms - calculated osms of non-gap acidosis, i.e., RTA Calculated osm = $(2 \times Na) + (gluc/18) +$ (BUN/2.8) + (ETOH/4.6)

 $\sqrt{}$ if Δ HCO $_3^-$ is appropriate (is there another 1° metabolic disturbance?) "1 for 1": HCO $_3^-$ normally falls 1 for every 1 increase in AG AKA "Delta Delta" (Δ HCO $_3^-$ / Δ AG should be 1–2) If the HCO $_3^-$ is higher than predicted \rightarrow 1° met alkalosis present If the HCO $_3^-$ is lower than predicted \rightarrow 1° met non-gap acidosis

	Causes of AG Metabolic Acidosis ("KUSMALE")
Ketones	Beta hydroxybutyrate (β -OH) and acetoacetate (AcAc), due to DKA, alcoholic ketoacidosis (AKA), starvation ketoacidosis. Urine and blood ketones measure AcAc +/- acetone, not β -OH (unless specific blood test sent). Compared to DKA, AKA mainly \uparrow β -OH and may have negative ketone tests
Uremia	Due to accumulation of phosphates, sulfates
Salicylates	Causes metabolic acidosis from lactate and ketones and respiratory alkalosis due to CNS stimulation
Methanol	Due to formate accumulation. Causes blurry vision + osmolar gap
Alcohols	Ethanol, Isopropyl alcohol. Alcohols metabolize to organic acids. Early $+$ osmolar gap no AG \rightarrow late $+$ AG, no osmolar gap
Lactate	↑ due to overproduction by anaerobic metabolism and underuse Type A: impaired tissue oxygenation (e.g., sepsis, ischemic bowel, CO, Sz) Type B: no impairment in oxygenation (e.g., malignancy, liver failure, thiamine deficiency, medications: NRTIs, metformin, linezolid) D-lactate: byproduct of bacterial metabolism, may → AG in short-gut syndrome, patients with h/o gastric bypass, small-bowel resection
Ethylene Glycol	Ethylene glycol → altered MS, renal failure, cardiopulmonary failure. + osmolar gap. Calcium oxalate crystals in urine; glycolate in serum

→ If osmolar gap >10, suspect ingestion

(methanol, ethylene glycol)

^{*}Less common causes: propylene glycol, paraldehyde, phenformin, ASA, cyanide, Fe, INH, toluene. ↓ AG consider unmeasured cations (↓ albumin, Li, Ca, Ig from MM, Mg, halide intoxication)

Causes of Non-AG	Metabolic Acidosis ("U.S.E.D. C.A.R.S.")*		
Ureterosigmoidostomy Colonic Cl ⁻ /HCO ₃ ⁻ exchange			
Saline	Large volume crystalloid resuscitation e.g., early goal directed therapy with saline or in DKA		
Early renal failure	Due to impaired HCO ₃ ⁻ generation		
Diarrhea	GI loss of HCO ₃ ⁻ (also pancreatic fistula)		
Carbonic anhydrase inhibitors	Causes renal H ⁺ retention, HCO ₃ ⁻ excretion		
Amino Acids	Arginine HCl, lysine		
RTA	See table below		
Supplements	TPN (excess chloride vs. acetate)		

^{*}Recent (resolved) respiratory alkalosis can cause persistent metabolic acidosis as kidneys need time to readjust.

	Types of RTA	s		
Type of RTA	Problem	UAG	Urine pH	Serum K
I (Distal)	Impaired H ⁺ (i.e., NH ₄ ⁺) excretion in collecting tubules	+	>5.3	1
II (Proximal)	HCO ₃ ⁻ loss, usually Fanconi's Syndrome of prox tubule with loss of glucose, phosphates, protein in proxi- mal tubule (causes: MM, acetazolamide, ifosfamide)	+ or –	<5.3 (except if receiving bicarb load)	1
IV (↓ Aldosterone)	Aldosterone deficiency (e.g., from low renin in diabetic nephropathy, adrenal insuff) or tubular resistance to aldosterone (e.g., K-sparing diuretics)	+	<5.3	1

Case Examples of Metabolic Acidosis		
Case	Interpretation	Diagnosis + Possible Scenario
pH 7.2, P _a CO ₂ 26, Na ⁺ 132, Cl ⁻ 97, HCO ₃ ⁻ 10	pH low, so acidemia. P_aCO_2 low, so metabolic. $HCO_3^-\downarrow$ by 14, $P_aCO_2\downarrow$ by 14, expected response. AG 25 (\uparrow by 15) and $HCO_3^-\downarrow$ by 14, so only 1 metabolic disorder	AG met acidosis
pH 7.35, P _a CO ₂ 35, Na ⁺ 140 , Cl ⁻ 100, HCO ₃ ⁻ 19	pH low, so acidemia. P_aCO_2 low, so metabolic. $HCO_3^-\downarrow$ by 5, $P_aCO_2\downarrow$ by 5 (expected). AG 21 (↑ by 11) and $HCO_3^-\downarrow$ by only 5 \rightarrow HCO_3^- higher than expected, so met alkalosis present	AG met acidosis and met alkalosis Lactic acidosis + severe vomiting
pH 7.47, P _a CO ₂ 20, Na ⁺ 140, CF 106, HCO ₃ - 14	pH high, so alkalemia. P_aCO_2 low, so respiratory. $P_aCO_2 \downarrow$ by 20, $HCO_3^- \downarrow$ by 10 (more than the 4 expected for acute), so met acidosis present since AG 20	AG met acidosis and resp alkalosis ASA intoxication

METABOLIC ALKALOSIS

Metabolic alkalosis is associated with \(\ \) mortality due to

- Cardiac arrhythmias
- Inhibition of hypoxic pulmonary vasoconstriction (worse V/Q matching)
- Depression of ventilation

Approach to Metabolic Alkalosis

- Determine if saline-responsive or resistant
 - Urine chloride is best indicator of volume status in setting of alkalemia (urine Na⁺ not reliable due to obligate cation losses when HCO₃⁻ is elevated)
 - Urine Cl⁻ < 20 suggests saline-responsive
 - Urine Cl⁻ > 20 suggests saline-resistant (unless patient is on diuretics)
- Correct metabolic alkalosis according to cause
 - Saline for hypovolemia
 - KCl if euvolemic (or less commonly HCl, arginine HCl, NH₄Cl). See Treatment of Severe Alkalemia
 - Acetazolamide if hypervolemic (e.g., contraction alkalosis with CHF)
 - Dialysis for severe, life-threatening alkalemia

Causes of Metabolic Alkalosis				
Saline-Responsive Saline-Resistant (Steroid exces				
Volume depletion -Due to vomiting, NGT, villous adenoma	Hypertensive: -Hyperaldosteronism -Cushing's			
Diuretic use / "contraction alkalosis" Diuresis → loss of HCO ₃ ⁻ poor fluid → extracellular fluid "contracts" around fixed	-Liddle's disease -Exogenous mineralocorticoids			
amount of $HCO_3^- \rightarrow \uparrow [HCO_3^-]$	Normotensive: -Hypokalemia (severe)			
Posthypercapnea -Recent respiratory acidosis, kidneys have not completely readjusted	-Milk alkali syndrome (exogenous alkali) -Bartter's/Gitelman's syndrome			

	Case Examples of Metabo	olic Alkalosis	
Case	Interpretation	Diagnosis + Possible Scenario	
pH 7.43, PaCO₂ 52, HCO₃ ⁻ 34	pH high, so alkalemia. P _a CO ₂ high, so metabolic. HCO ₃ ⁻ ↑ by 10, P _a CO ₂ ↑ by 12 (>7 so ↑ P _a CO ₂ due to resp alkalosis)	Metabolic alkalosis and respira- tory acidosis N/V and received opioid for abdominal pain	
pH 7.48, P _a CO ₂ 47, Na ⁺ 142 Cl ⁻ 98, HCO ₃ ⁻ 34, U _{Cl} 29	pH high, so alkalemia. P_aCO_2 high, so metabolic. $HCO_3^- \uparrow$ by 10, $P_aCO_2 \uparrow$ by 7 (expected "10 for 7"). $U_{Cl} > 20$, so not saline-responsive	Simple metabolic alkalosis, not saline-responsive Hyperaldosteronism or Cushing's Disease	

RESPIRATORY ACIDOSIS

P_aCO₂ reflects balance between CO₂ production (VCO₂) and alveolar ventilation (VA):

P_aCO₂ a VCO₂ / VA

VE (minute ventilation) = VA + VD (dead space ventilation), so therefore P_aCO_2 a VCO_2 / (VE – VD)

Hypercapnia results from:

- \downarrow VE due to \downarrow VT and/or \downarrow RR
- ↑ VD

• Rarely, \(\gamma \cong VCO_2\) (e.g., \(\gamma \cap \cap \) carb intake, exercise, fever) with all other things equal

	Causes of I	Respiratory Acidosis	
1."Won't Breathe'	,		
	Mechanism	Etiologies	Management
CNS Depression	↓ RR	Sedatives, head injury, brainstem stroke, CNS infection, response to metabolic alkalosis, hypothy- roidism	Stop/reverse sedatives (Naloxone 0.4 mg q2 min prn, Flumazenil 0.2 IV q1min up to 0.8 mg) Head CT if? intracranial process Intubate and ventilate
2."Can't Breathe"			
	Mechanism	Etiologies	Management
Neuromuscular Weakness	↓VT, Neg Insp Force (NIF) or Mean Insp Pressure (MIP) weaker than -25 cm H ₂ O	Neuropathies: ALS, polio, Guillain-Barre NM Junction: Myasthenia Gravis, botulism Myopathies: diaphragm weakness, PM/DM, muscular dystrophy, ↓↓ phosphate	√fluoroscopic "sniff test" for paradoxical eleva- tion of paralyzed diaphragm Treat underlying disorder, PT, nutrition, BiPap or ventilator support prn
Parenchymal or Airway Disease	↓VT and/or ↑ VD/VT (e.g., rapid shallow breathing)	Pneumonia, CHF, Restrictive lung dis- ease, ILD, COPD (usually FEV1 < 1L), Asthma	NIPPV can ↓ intubation in COPD, CHF (Lancet. 2000; 355:1931, Lancet. 2006;367:1155)
Thoracic Abnormalities	↓VT due to ↓ compliance	Chest wall: kyphosis, scoliosis, flail chest, obesity (likely also ↓ central drive) Pleura: effusions, pleural fibrosis, PTX	Treat underlying disor- der if possible Avoid causes of further ↓ ventilation (opioids, contraction alkalosis)

NM junction, neuromuscular junction; PM/DM, polymyositis/dermatomyositis; ILD, interstitial lung disease; NIPPV, non-invasive positive pressure ventilation.

- Respiratory stimulants (e.g., theophylline, medroxyprogesterone, acetazolamide) have not been shown to work except for naloxone in opioid overdose
- In COPD, O_2 therapy may \rightarrow hypercapnia via $\uparrow O_2$ in poorly ventilated lung units $\rightarrow \downarrow$ hypoxic vasoconstriction $\rightarrow \uparrow$ dead space $\rightarrow \uparrow P_aCO_2$ (*Lancet*. 2001;357:884)
- Permissive hypercapnia in ARDS: little evidence of harm: HR, CO, PVR transiently ↑, and some evidence of benefit: ↓ shunt, improved CO, better O₂ unloading by Hb, ? ↓ capillary leak (*AJRCCM*. 1997;156:1458, *Minerva Anesthesiol*. 2006;72(6):567)
- Avoid hypercapnia if \(\gamma\) ICP, right heart failure (may not tolerate pulmonary vasoconstriction (Am J Kidney Dis. 1997;30:561)), renal failure (unable to buffer pH)

Case Examples of Respiratory Acidosis			
Case Interpretation Diagnosis + Possible Sc			
pH 7.27, P _a CO ₂ 60, HCO ₃ - 27	pH low, so acidemia. PaCO₂ high, so respiratory acidosis. PaCO₂ ↑	Acute respiratory acidosis	
3	by 20, HCO ₃ ⁻ ↑ by 3 (close to 2, expected in acute resp acidosis)	Pulmonary edema with hypoven- tilation	

pH 7.3, PaCO ₂ 60, HCO ₃ ⁻ 29 Na ⁺ 132 Cl ⁻ 95	pH low, so acidemia. P _a CO ₂ high, so respiratory acidosis. P _a CO ₂ ↑ by 20, HCO ₃ ↑ by 5, which is more than the 2 expected for acute resp acidosis but <8 expected for chronic respiratory acidosis, so metabolic disorder may be present	Acute respiratory acidosis with concurrent metabolic alkalosis \$\rightarrow\$ RR due to opioids in a patient with pancreatitis and severe N/V OR
	OR Chronic resp acidosis, but HCO ₃ by less than the expected change of 8, so metabolic acidosis	Chronic respiratory acidosis with concurrent metabolic acidosis COPD patient with chronic CO ₂
	also present. AG is normal. OR	OR
	Chronic respiratory acidosis at baseline (P_aCO_2 50, HCO_3^- of 28), now with acute \uparrow of P_aCO_2 50 \rightarrow 60 and an expected \uparrow of HCO_3^- by 1	Acute on Chronic Respiratory Acidosis COPD patient with CO ₂ retention having an exacerbation
pH 7.22, P _a CO ₂ 48, HCO ₃ ⁻ 19 Na ⁺ 135 Cl ⁻ 100	pH low, so acidemia. P _a CO ₂ high so respiratory acidosis. P _a CO ₂ ↑ by 8, HCO ₃ ⁻ ↓ by 5. HCO ₃ ⁻ should ↑ for acute or chronic respiratory acidosis, so metabolic acidosis present. AG 16.	Respiratory acidosis and AG metabolic acidosis Pneumonia with hypoventilation and sepsis with lactic acidosis

RESPIRATORY ALKALOSIS

- Respiratory alkalosis has more cellular effects at given pH than metabolic alkalosis because P_aCO₂ equilibrates faster (*NEJM*. 2002;346(1):43)
- Respiratory alkalosis is a poor prognostic sign in critical illness, associated with higher mortality (*Acid–Base. Boston: Little, Brown.* 1982;349)
- Induced hypocapnia will transiently \downarrow ICP by decreasing cerebral blood flow and volume, but will also \downarrow O₂ delivery and may cause ischemia (*NEJM*. 2002;346(1):43)
- Hyperventilation and respiratory alkalosis \rightarrow bronchospasm and direct lung injury (*NEJM*. 2002;346(1):43)

Causes of I	Respiratory Alkalosis
Primary Hyperventilation	Secondary Hyperventilation (due to hypoxemia or pulmonary problem)
Pain, anxiety, fever CNS disorders affecting respiratory drive Drugs: ASA, progesterone, theophylline, beta agonists Pregnancy, sepsis, liver failure, mechani- cal ventilation	Asthma Pneumonia PE (can also $\rightarrow \uparrow$ PaCO2 with large \uparrow dead space with massive PE) Restrictive lung disease CHF (early)

Case Examples of Respiratory Alkalosis			
Case	Interpretation	Diagnosis + Possible Scenario	
pH 7.72, P _a CO ₂ 20, HCO ₃ ⁻ 25, Na ⁺ 135, Cl ⁻ 97	by 20, HCO ₃ ⁻ ↑ by 1	Mixed acute resp alkalosis and met alkalosis	
	(HCO ₃ ⁻ should ↓ for resp alk, so met alkalosis also present)	Pneumonia with dyspnea, fever, tachy- pnea and continuing to take diuretic	
pH 7.60, P ₂ CO ₂ 25, HCO ₃ ⁻ 24, Na ⁺ 148, Cl ⁻ 95	pH high, so alkalemia. P_aCO_2 low so respiratory. $P_aCO_2 \downarrow$ by 15, $HCO_3^- \downarrow$ by 0	Mixed resp alkalosis, AG met acidosis, met alkalosis	
	(should be lower, so met alk present). Also AG 29, so AG met acidosis present.	DKA with N/V and aspiration causing respiratory distress	

ASSESSING OXYGENATION BY ARTERIAL BLOOD GAS

- Most oxygen in the blood is bound to hemoglobin and a small fraction is dissolved gas. O_2 Content = $Hgb \times 1.36 \times SaO_2 + 0.003 \times PaO_2$
- A-a Gradient: difference between PAO₂ and PaO₂, measure of alveolar–capillary gas exchange (abnormal in shunt, VQ mismatch and diffusion defect)
- Oxygenation can be assessed by pulse oximetry (Hgb saturation) or PaO_2 . The relationship between O_2 saturation and dissolved O_2 is determined by the oxyhemoglobin dissociation curve (Figure 2)

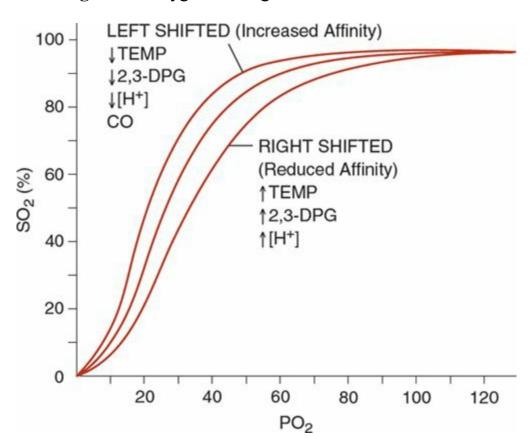


Figure 2. Oxygen-Hemoglobin Dissociation Curve

Source: Arterial Blood Gases in Clinical Methods: The History, Physical, and Laboratory Examinations. 3rd ed. Walker HK, Hall WD, Hurst JW, editors. Boston, MA: Butterworths; 1990.

• Acidemia, increased T, increased 2,3-DPG will shift the curve to the right and facilitate O₂

unloading to the tissues

- Alkalemia, low T, low 2,3-DPG (e.g., due to massive transfusions of stored blood, hypophosphatemia) and CO poisoning will increase the affinity of Hb to O₂ and shift curve to the left. This can lead to false reassurance from pulse oximetry.
- CO binds Hb tightly to form CO-Hb which does not carry O_2 (e.g., if COHb is 25% and Hb is 12, effective Hb is 9 and max SaO_2 is 75%). Pulse oximeter will falsely read 100% because COHb is red in color (classic "cherry red" patient). PaO2 will be normal. Diagnose by measuring CO level. Treat with 100% FiO_2 or hyperbaric O_2 to displace CO.
- Cyanide decreases peripheral O₂ extraction → increased SvO₂, SaO₂. PaO₂ will be normal. Patient is not cyanotic despite tissue hypoxia.
 - Calculate PAO_2 from alveolar gas equation: $P_AO_2 = FiO_2 \times (P_{atm}-P_{H2O}) P_aCO_2/R$
 - Normal A-a gradient is age/4 + 4

ANALGESIA, SEDATION, AND DELIRIUM

NATHAN E. BRUMMEL, MD • ALESSANDRO M. MORANDI, MD, MPH • E. WESLEY ELY, MD, MPH

GENERAL PRINCIPLES

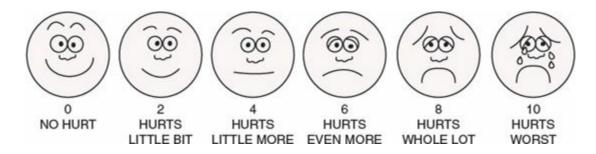
- Provide comfort, control pain, and anxiety without over sedation
 - Consequences of **under-treating**: patient suffering, device removal, ventilator dyssynchrony, myocardial ischemia
 - Consequences of **over-treating:** delirium, difficulty assessing neurologic function, prolonged mechanical ventilation (MV), immobility, ventilator associated pneumonia (VAP), increased hospital and ICU length of stay (LOS), adverse psychological outcomes (e.g., Post-Traumatic Stress Disorder)
- Interdisciplinary approach best (*Chest.* 2008;133:552)
 - Nursing bedside experience and frequent assessments
 - Pharmacist knowledge of medications and possible interactions
 - Physician integration of pain management and sedation into overall treatment plan
- Establish pain management and sedation **targets** using validated measures and **re-evaluate** frequently to ensure treatment is not under or over treating symptoms (pain or agitation)
- Integration of analgesia, sedation, and delirium monitoring/management preferred approach.

PAIN/ANALGESIA

Assessing Pain

- Pain assessment associated with short duration of MV, ICU LOS, and VAP (*Anesthesiology*. 2009;111:1308)
- Establish target for patient comfort and use pain scale to determine if pain at target
- Assessment Tools
 - Interactive Patients
 - Numerical Rating Scale (0 = "no pain" \rightarrow 10 = "worst pain ever")
 - Wong-Baker Visual Scale (smiling face = "no hurt"; crying face = "hurts worst") see Figure 1.

Figure 1. Visual Pain Scale



• Non-Interactive Patients

• **Behavioral Pain Scale (BPS):** 12-point scale incorporating facial expression, upper limb movements and compliance with mechanical ventilator. 0 points = no pain; 12 points = severe pain (*Crit Care Med.* 2001;29:2258)

	Behavioral Pain Scale	
ltem	Description	Score
	Relaxed	1
Facial	Partially tightened (e.g., brow lowering)	2
Expression	Fully tightened (e.g., eyelid closing)	3
•	Grimacing	4
	No movement	1
Hansa Parks	Partially bent	2
Upper Limbs	Fully bent with finger flexion	3
	Permanently retracted	4
Compliance	Tolerating movement	1
	Coughing but tolerating ventilation most of the time	2
with ventilation	Fighting ventilator	3
	Unable to control ventilation	4

• Surrogate raters/ Family members 79.9% sensitive and 67.7% specific assessing pain (*Crit Care Med.* 2000;28:1347).

Treating Pain

- In many cases, pain can be treated but not completely eliminated → treat to tolerance of pain
- Preventing pain is often more effective than treating established pain
- Pain may cause agitation → assessing and treating pain reduces need for sedatives (*Anesthesiology*. 2009;111:1308)
- Non-pharmacologic Interventions: reposition patient, remove irritating physical stimuli, apply heat/cold
- Analgosedation: analgesia based sedation → treat pain first, then use sedative, if necessary, to treat persistent agitation
 - Analgosedation strategy (1st line: morphine prn for pain, 2nd line: short-course (<6 hrs) propofol for persistent agitation) shortens duration of MV, ICU LOS, and hospital LOS. (*Lancet*. 2010;375:475)

• Pharmacologic Interventions:

- Non-opioid analgesics:
 - NSAIDs and acetaminophen may be used as adjuncts to opioids. Side effects (GI bleeding, renal toxicity, and hepatoxicity) limit use in ICU.
- Opioid analgesics:
 - IV administration provides quick onset but shorter duration of effect → more frequent dosing
 - Control pain with basal pain medication (scheduled or continuous) with as needed dosing for 'breakthrough' pain
- Start with bolus dosing, if needing >3 boluses/hr consider continuous administration
 - Renal and hepatic failure alter metabolism of opioids and/or prevent elimination → alter dosing to avoid prolonged effects.
- Elderly may have lower dosing requirements
 - Monitor level of sedation (see below). Perform daily interruption of continuous infusion and or hold bolus administration.

- All patients on opioids should receive bowel regimen (e.g., docusate 100–200 mg po BID)
- See table for commonly used opioids in the ICU

Select Opioid Analgesics				
Drug	Eqianalgesic Dose	Half Life	Intermittent Dose	Infusion Dose
Fentanyl	200 mcg	1.5–6 hrs	0.35-1.5 mcg/ kg q0.5-1-h	0.7–10 mcg/kg/hr
Morphine	10 mg	2–3 hrs	0.01-0.15 mg/ kg q1-2-h	0.07-0.5 mg/kg/hr
Hydromorphone	1.5 mg	3–7 hrs	10-30 mcg/kg iv q1-2-h	7–15 mcg/kg/hr
Remifentanil	-	3–10 min	_	0.6–15 mcg/kg/hr

AGITATION/SEDATION

Agitation/Sedation Balance

• Agitation ≠ "sedation deficiency" → search for cause of agitation (e.g., hypoxemia, Endotracheal tube (ETT) malposition, discomfort from ETT, pain, pneumothorax, GI or bladder distention, ventilator dyssynchrony)

Assessing Level of Sedation/Agitation

• Use sedation scale Richmond Agitation Sedation Scale (RASS, see table) or Sedation-Agitation Scale (Riker/SAS, see table) to assess level of sedation

	Richmond	Agitation and Sedation Scale (RASS)	
Scale	Label	Description	
+4	Combative	Combative, violent, immediate danger to staff	
+3	Very Agitated	Pulls to remove tubes or catheters; aggressive	
+2	Agitated	Frequent non-purposeful movement, fights ventilator	
+1	Restless	Anxious, apprehensive, movements not aggressive	
0	Alert & Calm	Spontaneously pays attention to caregiver	
-1	Drowsy	Not fully alert, but has sustained awakening to voice (eye opening & contact >10 sec)	
-2	Light sedation	Briefly awakens to voice (eyes open & contact <10 sec)	
-3	Moderate Sedation	Movement or eye opening to voice (no eye contact)	
-4	Deep Sedation	No response to voice, but movement or eye opening physical stimulation	
-5	Unarousable	No response to voice or physical stimulation	

(JAMA. 2003;289:2983, AJRCCM. 2002;166:1338)

Riker Sedation-Agitation Scale (SAS)				
Scale Label		Description		
7	Dangerous agitation	Pulling at ET tube, trying to remove catheters, climbing over bed rail, striking at staff, thrashing side-to-side		
6	Very agitated	Does not calm, despite frequent verbal reminding of lin requires physical restraints, biting ET tube		
5	Agitated	Anxious or mildly agitated, attempting to sit up, calms down to verbal instructions		
4	Calm and cooperative	Calm, awakens easily, follows commands		
3	Sedated	Difficult to arouse, awakens to verbal stimuli or gentle shaking but drifts off again, follows simple commands		
2	Very sedated	Arouses to physical stimuli but does not communicate of follow commands, may move spontaneously		
1	Unarousable	Minimal or no response to noxious stimuli, does not communicate or follow commands		

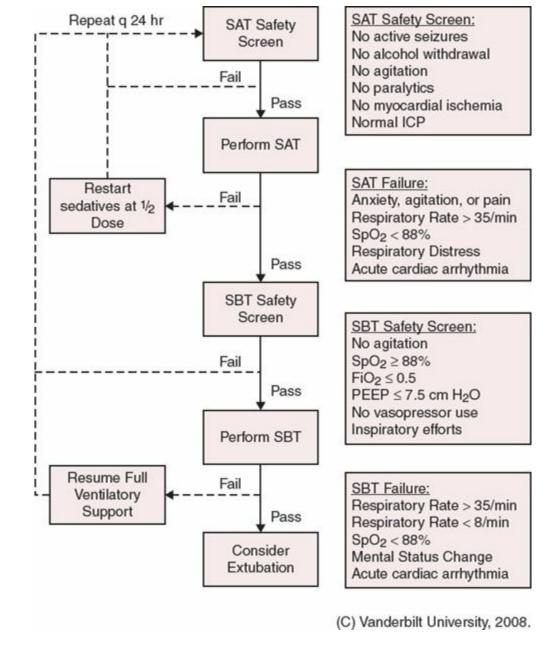
(Crit Care Med. 1999;27:1325)

- Establish target level of sedation \rightarrow most patients can be alert and calm (e.g., RASS 0, Riker 4)
- Keep patient at target level of sedation → decrease amount of sedative if over-sedated, increase amount of sedative if under-sedated/agitated. Reassess frequently (every 4–6 hrs).
- Analgesics may be enough to provide adequate level of sedation, see Analgosedation.

Principles of Sedation Management:

- Use intermittent bolus rather than continuous infusion (*Chest.* 1998;114:541)
- If >3 boluses/hr, consider continuous infusion.
- Use of daily "spontaneous awakening trial" (SAT) → shortens duration of mechanical ventilation, ICU & hospital LOS (*NEJM*. 2000;342:1471; *Lancet*. 2008;371:126).

Figure 2. "Wake up & Breathe Flowchart" Integration of Spontaneous Awakening Trials (SAT) and Spontaneous Breathing Trials (SBT)



• Performing the SAT:

Step 1: Screen patient for: sedation given for EtOH withdrawal, increasing agitation, paralytics, myocardial ischemia in last 24 hrs, or elevated ICP. If any are present, do not perform SAT.

Step 2: Hold bolus analgesics/sedatives and/or stop continuous infusions.

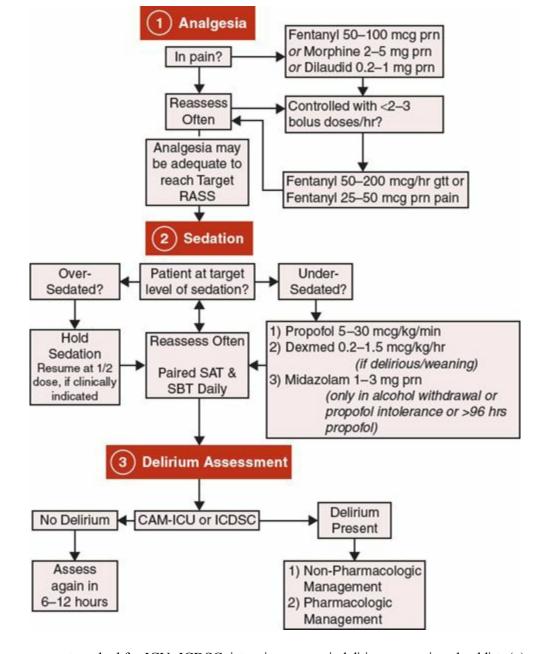
Step 3: SAT 'pass' = RASS -3 to +1 or Riker 3 to 5. SAT 'fail' = RASS +2 to +4 or Riker 6 or 7.

If pass *SAT*: proceed to spontaneous breathing trial (SBT).

If fail SAT: if necessary, resume analgesia/sedation at ½ previous dosing.

- Paired "awake and breathing" strategy (daily SAT + SBT) → shorter duration of mechanical ventilation, ICU & hospital LOS and 14% improved mortality at 1 yr. (*Lancet.* 2008;371:126)
- Use of an analgesia-sedation management protocol → shorter duration of mechanical ventilation, ICU LOS, and hospital LOS (*Crit Care Med.* 1999;27:2609). (see Figure 3)

Figure 3. Analgesia-Sedation Protocol



CAM-ICU, confusion assessment method for ICU; ICDSC, intensive care unit delirium screening checklist. (c) www.icuderilium.org.

• Avoid benzodiazipines as first or second line sedative agents (except in EtOH withdrawal) → Benzidiazepines are associated with higher rate of delirium and prolonged mechanical ventilation (*Crit Care Med.* 2006;34:1326; *JAMA.* 2009;301:489; *Anesthesiology.* 2006;104:21).

Drug	Mechanism of Action	Half Life	Intermittent Dose	Infusion Dose
Propofol	GABA _a agonist	40 min	0.2-0.6 mg/kg	5–80 mcg/ kg/min
Dexmedetomidine	CNS α ₂ agonist	6 min	_	0.1–1.4 mcg/kg/hr
Haloperidol	CNS D ₁ & D ₂	18 hrs	2-10 mg (iv)	0.04-0.15 mg/kg/hr
Midazolam	GABA _a agonist	3 hrs	0.02-0.08 mg/kg	0.04-0.2 mg/kg/hr
Lorazepam	GABA _a agonist	8 hrs	0.2-0.06 mg/kg	0.01-0.1 mg/kg/hr

DELIRIUM IN THE ICU

- Acute disturbance of consciousness that develops over a short period of time (hours to days) and fluctuates over time and is usually reversible.
- Affects 60%–80% of mechanically ventilated patients and 40%–60% of non-ventilated patients
- ICU Delirium associated with triple the risk of death 6 mos post-critical illness
- Delirium associated with poor long-term cognitive and functional outcomes
- www.icudelirium.org

Pathophysiology

- Neurotransmitter imbalance (ACh deficiency, dopamine excess)
- Inflammation (TNF-alpha, IL-6)
- Impaired oxidative metabolism (low cerebral perfusion, hypoxemia)
- Changes in large neutral amino acids concentrations (neurotransmitter precursors & toxic metabolites)
- Primed microglia → overactivation due to cytokines (e.g., TNF-alpha) → neuroinflammation

Risk Factors

• Average ICU patient has 10+ risk factors for delirium (*Intensive Care Med.* 2001; 27:1892) (see Table below)

	Risk Factors for ICU Delirium		
Host Factors (Unmodifiable)	Related to Critical Illness (Potentially Modifiable)	latrogenic (Modifiable)	
Age (elderly)	Metabolic derangements (acidosis, electrolyte disorders)	Medications (opioids & benzos)	
Alcoholism/Drug Use	Anemia	Immobility	
APO-E4 polymorphism	Infection/Sepsis	Sleep depravation	
Dementia/Mild Cognitive Impairment	Hypotension	>3 infusing medications	
Depression	Hypoxemia	Restraints	
Hypertension	Severity of illness	Open ICU room	
Smoking	Intracranial processes	Lack of visible daylight	
Vision/hearing impairment	Urinary/Fecal retention	Lack of visitors	
Malnutrition	Fever		

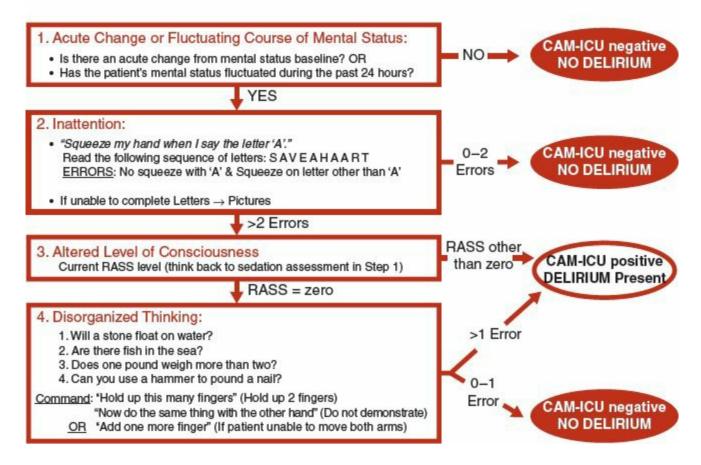
Delirium Diagnosis

- Three subtypes (*J Am Geriatr Soc.* 2006;54:479)
 - Hyperactive (5%): agitated or combative.
 - Hypoactive (45%): lethargic, drowsy, infrequent spontaneous movement
 - Mixed (55%): features of both.
- Subsyndromal delirium: some features of delirium, but not the full clinical syndrome (*Intensive Care Med.* 2007;33:1007)
- Most delirium is mixed/hypoactive → often missed if not screened for.
- Validated Delirium Screening Tools:

Confusion Assessment Method for the ICU (CAM-ICU) (93% spec; 89% sens) (JAMA.

Figure 4. Confusion Assessment Method for the ICU (CAM-ICU)

DELIRIUM ASSESSMENT



(c) 2002, E. Wesley Ely, MD and Vanderbilt University, all rights reserved.

- 90% of CAM-ICU assessments take <1 min
 - Two step process:

Step 1: Assess level of consciousness using RASS Table

• If RASS -4 or -5, the patient is too sedated to assess for delirium, if -3 to +4, proceed with step 2.

Step 2: Assess for features of delirium:

Feature 1: Acute mental status change/fluctuation in mental status?

• Feature 1 present if mental status changed from baseline or fluctuation in mental status in last 24 hrs?

Feature 2: Inattention

- Cardinal feature of delirium → if attentive, patient does NOT have clinical delirium
- Assess via Attention Screening Exam:
 - 1) Say to the patient "Squeeze my hand when I say the letter 'A"
 - 2) Read the following letters, 1 sec apart: S-A-V-E-A-H-A-A-R-T
- Error if no squeeze on A or squeeze on letter other than A
- Feature 2 present if >2 errors

Feature 3: Altered level of consciousness?

• Feature 3 present if patient is any RASS except 0

Feature 4: Disorganized thinking?

- Ask patient these yes/no questions:
 - 1) "Will a stone float on water?"
 - 2) "Are there fish in the sea?"
- 3) "Does 1 pound weigh >2?"
- 4) "Can you use a hammer to pound a nail?"
- Feature 4 present if >1 wrong answer
- A patient is delirious (CAM-ICU positive) if Features 1 **AND** 2 and *either* Feature 3 **OR** Feature 4 are present.

Intensive Care Unit Delirium Screening Checklist (ICDSC) (Intensive Care Med. 2001;27:859)

- Eight-item screening tool based off information from last 8–24 hrs.
- Score of >4 99% spec; 64% sens for delirium

Checklist Item	Description	
Altered level of consciousness*		
A	No response	
В	Response to intense and repeated stimulation	
С	Response to mild or moderate stimulation	
D	Normal wakefulness	
E	Exaggerated response to normal stimulation	
Inattentiveness	Difficulty following instructions or easily distracted	
Disorientation	To time, place or person	
Hallucination-delusion-psychosis	Clinical manifestation or suggestive behavior	
Psychomotor agitation or retardation	Agitation required use of drugs or restraints or slowing	
Inappropriate speech or mood	Related to events or situation or incoherent speech	
Sleep/wake cycle disturbance	Sleeping <4 hrs/d, waking at night, sleeping all day	
Symptom fluctuation	Symptoms of above occurring intermittently	
Total Score (one point for obvious presence of features above)	0–8	

^{*}If level of consciousness A or B no other features are assessed that day.

• If delirium diagnosed, "THINK" about causes and management (see Table below)

	"THINK" Mnemonic for Delirium Causes and Management
Т	 Toxic Situations CHF, shock, dehydration Deliriogenic Medications (e.g., anti-cholinergics or benzodiazipines) New organ failures: e.g., liver or kidney Tight Titration of sedatives & analgesics
Н	Hypoxemia Haloperidol or other antipsychotic for treatment
I	Infection/Sepsis (nosocomial) Immobility
N	Non-pharmacoloic interventions Hearing aides & glasses Reorientation, Sleep protocol Music Noise control Ambulation
K	K+ or other electrolyte abnormalities

(Neurotherapeutics, 2012;9:158-175)

Delirium Management

• Non-pharmacologic:

- 40% reduction in incidence of delirium in non-ICU patients with multi-component protocol: reorientation, removal of restraints and catheters as quickly as possible, mobilization, hydration, eyeglasses and hearing aids (*NEJM*. 1999;340:669).
- Early mobility and PT/OT (<72 hrs after ICU admission) → reduced ICU delirium duration by 50% (*Lancet*. 2009;373:1874)

• Pharmacologic:

- No FDA approved drugs for treatment.
- Benzodiazipines not indicated (except for delirium tremens) and may worsen delirium
- Typical and atypical antipsychotics commonly used despite no randomized controlled trials demonstrating efficacy (*Crit Care Med.* 2009;37:825–32)

• Typical Antipsychotics*

- Haloperidol: 2–5 mg PO or IV q6h, once calm, use lower doses; in elderly use ½ dose. Doses >20 mg/d increased risk of adverse effects: dystonic reactions, oversedation, malignant hyperthermia, EPS, and QTc prolongation)
- Atypical Antipsychotics* (may reduce serious adverse effects: data mixed regarding efficacy)
 - Olanzapine: 5 mg PO or SL daily; in elderly use ½ dose.
 - Risperidone: 0.5 mg PO twice daily. Max dose 2.5 mg/d.
 - Quetiapine: 25–50 mg PO q12h; titrate to effect q24.
- *Monitor QTc; discontinue drug if baseline ≥450 ms or prolonged from baseline >25%
- **Sedation Strategy:** Dexmedetomidine (vs. benzodiazipines) reduces duration of ICU delirium (*JAMA*. 2009;301:489 and *Crit Care Med*. 2010;14:R38).

Integrating Analgesia, Sedation and Delirium: "ABCDE" Approach (*Chest.* 2010;138:1224) (see Table below)

• "Bundled" evidence based therapies individually shown to reduce ventilator time, delirium, functional impairments and death.

	"ABCDEs" for Analgesia, Sedation and Delirium
A,B,C	Awakening trial and Breathing trial Coordination, emphasizing interdisciplinary care
С	Choose appropriate sedation strategy (protocols, analgosedation and avoidance of benzodiazipines)
D	Delirium Monitoring and Management
E	Early mobility and physical rehabilitation

NUTRITION

MARCUS D. DARRABIE, MD • DANNY O. JACOBS, MD, MPH

Significance

- World Health Organization defines malnutrition as the cellular imbalance between the supply of nutrients and energy and the body's demand for them to ensure growth, maintenance, and specific functions
- 25–50% of hospitalized patients are malnourished (Arch Intern Med. 1987;147(8):1462)
- Severe illness generally leads to a catabolic state, that can be aggravated by inadequate intake of protein and energy
- Immobilization, sedentarism, as well as age exacerbate loss of lean body mass
- Severe stress and malnutrition are associated with negative energy balance
- Early recognition of malnutrition is clinically important since ongoing malnutrition can exacerbate organ dysfunction by depleting protein in bodily tissues
- Experimental studies in animals have shown early nutrition to reduce septic morbidity, reduce bacterial translocation and reduce infectious complications, whether the same effects occur in humans is controversial (*J Trauma*. 1995;39(1):44)
- Optimal nutrition management may facilitate recovery of hospitalized patients

Nutritional Assessment

- History & physical, laboratory tests or as percentage of weight change
- A subjective global assessment screen may be used to evaluate nutritional status and identify malnourished patients (*JPEN J Parenter Enteral Nutr.* 1987;11(1):8)
 - Weight change (overall and change in past 2 wks)
 - Dietary intake (relative to normal weight)
 - Gastrointestinal symptoms (none, nausea, or vomiting)
 - Functional capacity (no dysfunction, or dysfunction and duration)
 - Physical appearance (subjective assessment of fat loss, muscle wasting, edema and ascites)
 - Nutritional status classified as well nourished (SGA A), moderately malnourished (SGA B), or severely malnourished (SGA C)
- Anthropometric data (weight, height, tricep skinfold thickness) correlates well with body composition in large epidemiologic survey studies
 - Ideal Body Weight (men) = $50 \text{ kg} + 2.3 \text{ kg} \times (\text{Height (in.)} 60)$ Ideal Body Weight (women) = $45.5 \text{ kg} + 2.3 \text{ kg} \times (\text{Height (in.)} - 60)$

	Classification of Malnutri	tion
Degree of Malnutrition	Percentage of Ideal Body Weight (Current Weight/Ideal Body Weight × 100)	Percentage of Usual Body Weight (Current Weight/Usual Weight × 100)
Mild	80%-90%	85%-95%
Moderate	70%–79%	75%-84%
Severe	0%-69%	0%-74%

Source: JPEN. 1977;1(1):11-22.

- Major acute changes in weight likely represent changes in fluid status
- Though not seen in its pure form in hospitalized patients, chronic deficits in protein, or energy intake lead to protein—energy malnutrition, which can be broadly classified as follows:
 - Marasmus-type
 - Acceptable ratio of protein: calorie intake but inadequate total dietary calories
 - Preserved visceral proteins (short lived proteins mostly synthesized in the liver such as albumin, pre-albumin, retinol binding protein)
 - May manifest as impaired immunity (i.e., decreased total lymphocyte count and positive skin test anergy)
 - Typical patient may appear with wasting of both muscle and fat (i.e., cachexia, sunken supraclavicular fossae, temporal wasting, muscle pain)
 - Kwashiorkor-type
 - Adequate calorie but insufficient total protein intake
 - Reduction in visceral proteins
 - Typical patient may have evidence of increased extracellular fluid (i.e., anasarca, ascites, decreased skin turgor, liver enlargement, parotid gland hypertrophy)

	Clinical Signs of Malnutrition	1
Location	Signs	Deficiencies
Hair	alopecia, brittle color change, dry- ness, easy pluckability	Protein-calorie Malnutrition, Biotin, Zinc Vitamins E and A
Skin	acneiform lesions, follicular kerato- sis, xerosis, ecchymosis, intrader- mal petechia, erythema, hyperpig- mentation, scrotal dermatitis	Vitamin A, Vitamin C or K, Niacin
Eyes	angular palpebritis, bitot's spots, conjunctival xerosis	Vitamin B ₂ , Vitamin A
Mouth	angular stomatitis, atrophic papil- lae, bleeding gums, cheilosis, glossi- tis, magenta tongue, loss of taste	Zinc,Vitamin B ₁₂ , Niacin, Vitamin C,Vitamin B ₂
Extremities	genu valgum or varum, loss of deep tendon reflexes of the lower extremities	Vitamin D,Vitamins B ₁ and B ₁₂
Neurologic	symmetric motor or sensory dys- function, ataxia, nystagmus, heart failure, mental status changes or confusion	Thiamine
Musculoskeletal	muscle and fat wasting, weakness, muscle pain, heart failure (cardiomyopathy)	Selenium, Protein-Calorie Malnutrition

Source: Adapted in part from Bernard, MA, Jacobs, DO, Rombeau, JL. Nutrition and Metabolic Support of Hospitalized Patients. WB Saunders, Philadelphia, 1986.

- Nutritional monitoring should include daily fluid balance evaluation, daily weight, nitrogen balance determination as needed and testing for visceral protein status
- Biochemical markers of malnutrition and metabolic stress include:
 - Pre-albumin levels decrease acutely in malnutrition (half-life, 2 d)
 - Transferrin levels decrease in malnutrition (half-life, 8–10 d)
 - Thyroxine-binding pre-albumin levels decrease acutely (half-life, 1–2 d)
 - Retinol binding protein levels decrease acutely in malnutrition (half-life, 10 hr)

- Albumin levels may decrease with chronic malnutrition or may reflect conditions other than malnourishment and may be normal in some patients with protein—calorie malnourishment like kwashiorkor; additionally it is a strong indicator of operative risk but performs poorly as a nutritional marker (half-life, 20 d)
- C-reactive protein positive acute phase reactant increases in inflammation, decreases in malnutrition (half-life, 19 hrs)
- Electrolyte levels, magnesium, phosphorus, calcium, liver function tests, blood urea nitrogen, and creatinine assays

Most practitioners use pre-albumin, albumin, and transferrin as biochemical protein markers

Nutrition Requirements

Energy Expenditure

- Determination of energy expenditure is used to decide feeding regimen
- Nutritional requirements and energy expenditure can be measured or estimated by predictive formula
- Calculated or predicted energy expenditure is typically based on body size and a correction factor for metabolic stress is often used
- Basal energy expenditure (BEE): amount of energy produced per unit of time under basal conditions (i.e., complete rest, shortly after awakening, after 14-hr fast)
 - Most recognized calculation of BEE is the Harris-Benedict Equation
 - BEE (Males): 66 + 13.7 (weight in kg) + 5 (height in cm) **1**6.8 (age in years)
 - BEE (Females): 655 + 9.6 (weight in kg) + 1.8 (height in cm) 14.7 (age in years)
- Harris-Benedict equation and many other predictive equations may overestimate or underestimate nutritional needs in critically ill, overweight, and underweight patients

A modification of the HBE that is generally more applicable in the ICU is simply: BEE $(kcal/d) = 25 \mbox{ } \mbox{Ψ}$ weight (kg)

- Metabolic stress increases keal requirements as follows:
 - Thermal Injury (typically the greatest increase in BEE)
 - 0%–20% body surface area BEE × 1.0–1.5
 - 20%–40% body surface area BEE \times 1.5–1.85
 - 40%-100% body surface area BEE $\times 1.85-2.05$
 - Fever: BEE × 1.1 (for each unit of temp in °C greater than normal body temp)
 - Peritonitis: BEE × 1.2–1.5
 - Major sepsis: BEE × 1.4–1.8
 - Major Soft Tissue Trauma: BEE × 1.1–1.4
 - Multiple Long Bone Fractures: BEE × 1.2–1.4
- ullet Indirect calorimetry: a way to determine energy expenditure which utilizes measurements of CO_2

production and O₂ consumption in a closed ventilator system to provide an indirect estimate of caloric needs of hospitalized patients.

- Measured over 15–30 min period then extrapolated over a 24-hr period
- Hypermetabolism > 100% of predicted energy expenditure
- Normometabolism = 90%–100% of predicted energy expenditure
- Hypometabolism < 90% of predicted energy expenditure
- Respiratory quotient (RQ): ratio of CO₂ production and O₂ consumption; provides a rough estimate of substrate utilization during indirect calorimetry
 - $RQ = VCO_2/VO_2$

Energy	Sources and	d Associated Res	oiratory Quotients	
Substrate	Energy (kcal/g)	O ₂ Consumption VO ₂ (L/g)	CO ₂ Production VCO ₂ (L/g)	RQ
Ethanol	7.0	1.46	0.98	0.71
Fat oxidation	9.0	1.96	1.39	0.71
Protein oxidation	4.0	0.94	0.75	0.82
Carbohydrate Oxidation	4.0	0.81	0.81	0.9–1.0

Source: Adapted from Bernard, MA, Jacobs, DO, Rombeau, JL. Nutrition and Metabolic Support of Hospitalized Patients. WB Saunders, Philadelphia, 1986.

- In general RQ >1 indicates excessive calorie load and suggests that a reduction in caloric intake may be indicated
 - RQ \geq 1 indicates a need to decrease carbohydrates or lipids (*JPEN*. 2003;27(1):21–26.)
 - RQ < 0.82 indicates a need to increase caloric intake
 - RQ can equal 1.0 after eating; In diabetes RQ = 0.71; In starvation RQ = 0.83
- Protein intake requirements can generally be estimated as follows:
 - Healthy non-stressed metabolism: $0.8-1.0 \text{ g/kg/d} \times \text{weight (kg)}$
 - Mild-to-severe malnutrition and catabolic stress: 1.0–1.6 g/kg/d × weight (kg)
- Nitrogen balance measurements allow for a more specific assessment of the need for protein repletion
- Nitrogen balance can be estimated as follows: $(N_{in} N_{out}) = ([protein (grams)/6.25]-[24 hr Urine Nitrogen (grams) + 4 (grams)])$
 - Positive nitrogen balance is indicative of anabolism
 - Negative nitrogen balance is indicative of catabolism
- Nitrogen balance is improved with optimization of the non-protein calorie to nitrogen ratio
 - Normal adults during nitrogen equilibrium typically require 1 g nitrogen per 300 kcal
 - Critically ill patients require 1 g nitrogen per 150 kcal
 - 1 g nitrogen yields 6.25 g protein (i.e., a critically ill patient with a 1,750 kcal energy requirement may require 11.7 g nitrogen or 72.9 g protein)

Nutritional Support Routes

Determination of energy needs or requirements \rightarrow functional GI tract that can be used safety \rightarrow determination of optimal route: Oral vs. Enteric feeding tube

Determination of energy needs or requirements \rightarrow non-functional GI tract \rightarrow consider TPN if expected length of time is at least 7 days without feeding \rightarrow assess for placement of access device

Functional GI Tract – Enteral Nutrition

- The gut of postoperative, trauma, or nonsurgical critically ill patients is often functional and enteral is indicated if it can be used safely
- Approx 100 cm of small bowel is required for adequate nutrient absorption
- Advantages:
 - Reduced cost, more physiologic
 - Animal studies demonstrate reduced mucosal atrophy, reduced bacterial translocation and improved GI immunity (*J Trauma*. 1995;39(1):44)
- Potential contraindication(s) may include:
 - Ischemic bowel, bowel obstruction, hemodynamic instability, ileus, high output fistula, improper airway protection
- Typical Enteral Formulations (The exact formulas available vary by hospital; review of institutional formulations are required)

	Enteral Formulas	3
Enteral Formulas	Description	Examples
Standard	Mimics American diet, 50%–60% calories from carbs, 10%–15% from protein, 25%–40% from fat.	Isosource, Osmolite, Boost, Ensure
Concentrated	Similar to standard but density per milliliter is greater. Typically used for patients with fluid restrictions.	Ensure Plus, Impact 1.5, Twocal HN, Nutren Renal, Nutren 2.0
High nitrogen- protein	Contain >15% of calories by nitro- gen and protein. Typically used for patients with higher than normal protein needs.	Isosource HN, Osmolite HN, Replete, Boost HP, Peptamen VHP, Ensure HP, Promote
Elemental	For patients with impaired pancreatic and small bowel function. Consists of low residue, partially digested and easily absorbed proteins.	Alitraq, Peptamen, Vivonex PLUS, Vivonex T.E.N.
Fiber- containing or blenderized formulas	Contain fiber supplied from added soy or natural food sources. Intended to regulate bowel function by eliminat- ing diarrhea and constipation	Jevity, Compleat, Ensure with Fiber, Promote with Fiber, Nutren 1.0 Fiber

• Glutamine is the primary source of energy for enterocytes and helps maintain the integrity of bowel mucosa in animals. Its administration may be associated with decrease risk of infection in surgical patients (*World J Gastroenterol*. 2006;12(46):7537)

Enteric Access Routes

- Short-term feedings (<4 wks)
 - Oroenteric orally placed gastric or enteric tube, maybe favored in patients with nasal or facial injury
 - Nasogastric most common, typically large caliber, pre-pyloric placement

- Nasoenteric tube typically small caliber, post-pyloric placement
- Long-term feedings (generally recommended for feeding >4–6 wks) require placement of a more permanent gastrointestinal access
 - Percutaneous enteral device (gastric, gastric jejunal, or direct jejunal)
 - Surgically placed tube (gastrostomy or jejunostomy)
 - Endoscopic or radiographically placed in anatomically challenging cases

Enteric Feeding Protocols

- Tube position should be confirmed either directly or radiographically
- Patients should be placed upright at 30–45 degree positions
- Tubes should be flushed with at least 30 ml of water every 4 hrs to maintain patency; however, this may be adjusted-based on free water requirements
- Bolus feedings generally are given in 4-hr intervals via nasogastric or gastrostomy tubes with adjustments for gastric residual volume (i.e., tube feedings are typically held if residual is greater than volume of last bolus)
- Continuous feedings are typically administered via jejunal feeding tubes and may be administered over the entire day or given intermittently
- Small bowel feedings should be initiated at a slow rate (i.e., 15–25 cc/hr for continuous feedings) and advanced at a slow and fixed rate until reaching goal feeding rate
- No significant difference in aspiration risk between stomach and proximal duodenal feeding but aspiration events are less severe on average with feedings beyond the ligament of Treitz (Crit Care. 2003;7:R46)

Non Functioning GI Tract – Parenteral Nutrition

- Total parenteral nutrition (TPN) delivers nutrients via a hyperosmolar solution delivered into a central vein (typically superior vena cava)
- Indicated in critically ill, malnourished patients with contraindications to enteral feedings; initiated only if duration of therapy is anticipated to be >7 d
- Indications per ASPEN guidelines (JPEN. 2010;34(4):366) include:
 - Previously healthy patients with no evidence of protein calorie malnutrition if enteral nutrition is not feasible after 7 d of hospitalization
 - Protein calorie malnutrition upon admission with no enteral feeding options
 - Severely malnourished patients, prior to major upper GI surgery with no enteral feeding options
- Other indications include:
 - nonfunctioning gastrointestinal tract
 - short gut
 - prolonged need for bowel rest (typically >14 d)
- TPN formulations consist of dextrose, amino acids, lipids, vitamins, trace minerals, and elements
- Commercially available dextrose solutions range from 5% to 70% (i.e., D5W = 50 g dextrose/l, D70W = 700 g/l)
- Amino acid preparations consist of crystalline protein and synthetic amino acids with standard solutions ranging from 3% to 10%
- Fat solutions are isotonic and can be administered peripherally or centrally without concern for thrombosis. (typical products include: intralipid 10% and 20% composed from soybean, as well as Liposyn II 10% and 20% composed from safflower oil)
- Caution should be advised in the following instances of lipid administration:

- Fat solutions should be administered at no more than 2.5 g/kg/d and typically constitute 20%–30% of total calories
- Cautious administration to patients with respiratory distress syndrome, severe liver disease, or increased metabolic stress.
- Contraindicated in hypertriglyceridemia (>250 mg/kg), lipid nephrosis, egg allergy or acute pancreatitis.
- Other additives such as vitamins may be administered from commercially available preparations
- Trace minerals should be given in accordance with recommended daily allowance
- Give vitamin K separately and after evaluation of coagulation status: may jeopardize anticoagulation therapies such as warfarin (*Gastroenterology*. 2009;137:S105)
- Electrolytes are added to supplement deficits or achieve homeostasis

Typical Initiation Plan:

- Check all laboratory tests prior to initiation (glucose, magnesium, phosphorus, calcium bilirubin, SGOT, SGPT, alkaline phosphatase, BUN, serum creatinine)
- Determine fluid needs:
 - Holliday-Segar method = total daily volume requirement (cc/d) = 100 cc/kg for first 10 kg, 50 cc/kg for the second 10 kg, 20 cc/kg for each additional kg
 - Dextrose solutions provide 15%–35% final concentrations (150–350 g/l)
 - Typical amino acid solution range from 5% to 10% (50–100 g/l)
- Determine caloric and protein needs:
 - Calorie yield per gram of macronutrient
 - Fat 9.4 kcal/g; Protein 4.1 kcal/g; Carbohydrate 3.4 kcal/g
 - Total protein needs = $0.8-1.0 \text{ (g/d)} \times \text{weight (kg)}$
 - Total caloric needs = $25 \text{ (kcal/kg)} \times \text{weight (kg)}$
- Determine volume of lipid emulsion
 - 20%–30% of caloric intake is supplied by lipids; 2%–4% of total caloric needs should consist of essential fatty acids (i.e., linoleic acid and lipoprotein c)
 - Typical emulsions are provided in 10% and 20% concentrations in unit volumes of 50 cc preparations and yields 1.1 or 2.0 kcal/cc respectively
- Determine standard electrolytes, multivitamins, trace elements and other additives (i.e., H₂ blockers, Insulin)
- TPN requirements and tolerance should be assessed daily
- Goal rate is based on ability to tolerate glucose and fluid load (In general, patients should begin with 1 L on day 1, with advancement of 20–50 ml per hr)
- Optimal infusion of glucose ranges from 0.5 to 7.5 gm per kg per hr, maximum glucose oxidation occurs at an infusion rate of 5 mg/kg/min (*Ann Surg.* 1979;190(3):374)

TPN Electrolyte Amounts

Electrolyte Amounts in TPN

For a 70 kg male:

Fluid requirement: $100 (cc/kg) \times 10 + 50 (cc/kg) \times 10 + 20 (cc/kg) \times 50 = 2,500 cc or 2.5 l$

Estimated non-protein caloric requirement = $25 \text{ (kcal/kg)} \times 70 \text{ (kg)} = 1,750 \text{ kcal}$

Estimated lipid calories = $1,750 \times 20\% = 350$ kcal

Estimated dextrose calories = 1,750 - 350 kcal = 1,400 kcal

*Calculated protein requirement = 1.0 (g/d) \times 70 (kg) = 70 g or 70 g/2.5 l = 28.6 g/l

Calculated dextrose: 1,400 kcal/3.4 kcal/g = 411.8 g or 411.8 g/2.5 l = 164.7 g/l

Calculated lipid (20% intravenous solution) requirement = 350 kcal/2 kcal/ml \times 20% = 35 g or 35 g/2.5 l = 17.5 g/l

Final TPN formula = 28.6 g/l protein, 165 g/l of dextrose, 17.5 g/l intravenous lipids

Volume of 5% amino acid solution: 70 g/5% = 1,400 cc

Volume of 20% intravenous lipid: 350 kcal/2.0 kcal/cc = 175 cc

Volume of 50% dextrose (D50W) needed: 1,700 kcal per 1 l of 50% dextrose (500 g/l);

1,400 kcal/ 1,700 kcal/ 1 = .821 = 820 cc

50–100 cc may be added for electrolytes, additives, or trace vitamins and minerals

^{*}Debate exists regarding whether to count protein calorie intake.

Recommended Electrolyte Amounts			
Electrolyte	Recommended (Amount/d)	Typical Amount (mmol/l)	
Sodium	60-120 mEq	40-150 mmol/l	
Potassium	60-120 mEq	30-50 mmol/l	
Calcium	0-15 mEq	1.5-2.5 mmol/l	
Chloride	60-150 mEq	40-150 mmol/l	
Phosphorus	20-40 mmol	10-30 mmol	
Magnesium	0-25 mEq	5-10 mmol	
12 MVI Formula	10 ml		
Trace Element	5 ml		
Heparin	As needed		
Insulin	As needed		

Source: NEJM. 2009;361:1088-1097.

Source: NEJM. 2009;361:1088-1097.

- Complications of TPN:
 - Complications related to CV access catheter
- Metabolic problems include:
 - Increased blood glucose levels
 - Dehydration
 - Fatty liver

- Increased CO₂ production may lead to respiratory failure
- Nutritional complications include over and under feeding
- Combined Enteral-Parenteral Feeding:
 - Enteral nutrition as a sole route may result in under-feeding
 - Parenteral nutrition may result in overfeeding and associated metabolic and mechanical risks
 - Enteral feeding should be first option
 - Parenteral nutrition should be instituted if enteral nutrition is inadequate for caloric needs

Malnutrition Leading to Pulmonary Failure

- Too rapid re-feeding may lead to \downarrow PO₄ and respiratory compromise and is accompanied by:
 - Decreased vital capacity, minute volume, respiratory rate, tidal volume, and respiratory efficiency
 - Difficult weaning of mechanical ventilation due to impaired pulmonary reserve
 - Decreased phosphate, magnesium, sodium, and potassium stores
- Calorically dense formulations minimize fluid intake
- Serum phosphate levels (associated with decrease in hypoxic ventilatory response) should be routinely measured
- Patients with ARDS or acute lung injury may benefit from enteral feedings supplemented with omega 3 fish oils, and antioxidants (*JPEN*. 2010;34(4):366)

Renal Failure Leading to Malnutrition

- Patients may present with impaired electrolyte profiles, glucose intolerance and protein losses from hemodialysis
- Protein losses may be extremely high in renal failure requiring hemodialysis or continuous renal replacement therapy; therefore, these patients should not be placed on protein restricted diets
- Per ASPEN (*JPEN*. 2010;34(4):366) guidelines:
 - Patients receiving hemodialysis or renal replacement therapy may require between 1.5 g/kg/d and 2.5 g/kg/d of protein to achieve positive nitrogen balance or near nitrogen equilibrium
 - Renal specific nutrient formulations may be considered in patients with significant electrolyte abnormalities

Hepatic Failure Leading to Malnutrition

- Estimated 20% child-Pugh class A and 60% of child-Pugh class C have protein energy malnutrition
- Nutritional assessment may be difficult in decompensated cirrhotics due to changes in hepatic function and energy metabolism
- Simple bedside methods such as Subjective Global Assessment (battery of questions) or anthropometry can identify patients at risk
- Per ASPEN (*JPEN*. 2010;34(4):366) guidelines:
 - Standard enteral nutrition is the preferred route; however, parenteral nutrition is indicated when oral or enteral nutrition cannot sustain nutritional needs
 - Branched chain amino acid-enriched formulas may be used in encephalopathic patients refractory to antibiotic or luminal therapy

INFECTIOUS DISEASE, SEPSIS, AND THE SURVIVING SEPSIS GUIDELINES 2012

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EVALUATION OF NEW FEVER IN THE CRITICALLY ILL PATIENT

- Fever is very common in the ICU.
- Up to 40% of ICU patients experience a fever (temp >100.4°F) at least once during ICU course. (Crit Care Med. 2008;36(5):1531)
- Majority of fevers, particularly low-grade (<101.5°F) are of benign etiology and resolve without specific treatment. However, a minority of febrile episodes may be due to a serious or potentially life-threatening condition.
- Main objective is to distinguish infectious from non-infectious. (See Table)
- Approach to diagnosis should be tailored to patient and avoid unnecessary tests.
- Patients with fever and signs of sepsis, or who are at high risk of infection (e.g., immunocompromised patients) need empiric antibiotic treatment.

Selected Causes of ICU Fever			
Infectious	Non-Infectious		
Catheter infection Bacteremia VAP Sinusitis UTI Wound infection Endocarditis C. Difficile colitis	Post operative Transfusions Drug fever Thromboembolic disease Acalculous cholecystitis Cerebral hemmorrhage ARDS Adrenal insufficiency Thyroid storm Vasculitis Pancreatitis Hematoma Gout Alcohol withdrawl Tumor fever Burns		

VAP, ventilator-associated pneumonia; UTI, urinary tract infection; ARDS, acute respiratory distress syndrome.

NOSOCOMIAL INFECTIONS

Catheter-Related Blood Strem Infections (CRBSI) – also see Chapter 13.

Epidemiology

• Among most common of hospital-acquired infections.

• Attributable mortality anywhere from 12% to 25%.

Pathogenesis

- Microorganisms enter bloodstream via 1 of 4 mechanisms:
 - Colonization of the skin at the catheter entry site
 - Contamination of catheter hub or stopcock
 - Seeding of catheter through blood from infection at distant site
 - Contamination of intravenous infusates
- Short-term, noncuffed central venous catheters have highest rate of infection but arterial catheters and peripherally inserted central venous catheters (PICC lines) also cause infection at similar rates.

Clinical Manifestations

- Fever, rigors, hypotension, or other early signs of sepsis.
- Catheter entry sites and tunneled catheter tracts should be examined for erythema, local tenderness, or purulent drainage but most often are normal.

Microbiology of CRBSI

- Staphylococcus aureus and coagulase-negative Staphylococcus most common causative organisms.
- Assorted Gram-negative bacteria, *Enterococci* (including vancomycin-resistant enterococci) and *Candida* species make up remainder of infections.

Diagnosis

- Blood culture two sets from two different peripheral venous or arterial sites is definitive diagnostic test.
- In patient with intravascular catheter additional set drawn from the catheter may help in pinpointing catheter as source.
 - "Differential time to positivity" (>120 min) may distinguish between a line-related and a non-line-related bacteremia.
 - Semiquantitative cultures of tip may also point to catheter as source.

Treatment

- Antibiotics directed at typical pathogens should be started immediately and catheter should be removed (as soon as that can safely be done).
- Gram-positive organisms, including MRSA, cause the majority of infections and vancomycin is the first-line agent.
- In the immunocompromised or septic patient, empiric treatment should be broadened to cover typical nosocomial gram-negative organisms. Burn patients also at high risk for gram-negative infections. Fungal CRBSI, although increasing in incidence, is still relatively uncommon, and empiric antifungal coverage should be reserved for high-risk patients.
- After causative organism identified antibiotic therapy should be tailored.
- Exchange of an infected catheter over a guidewire is *not* effective for managing CRBSI. It would only be considered in cases when other sites for placement of a new catheter are not available and the catheter is essential and life saving.

Prevention

• Use maximum barrier precautions for placement procedure – sterile gloves, surgical mask and gown, and sterile drapes. Cleansing of skin with chlorhexidine superior to povidine–iodine.

- Access ports must be cleaned with an antiseptic immediately prior to use.
- Femoral insertion site should be avoided.
- Subclavian site is associated with a slightly lower risk of infection than internal jugular catheterization while it has a higher incidence of DVT and mechanical complications during placement.
- The longer an intravascular catheter stays in place the higher the risk of infection, but no evidence to support routine pre-emptive replacement of catheters. When no longer essential for care remove catheter immediately.

Ventilator Associated Pneumonia (VAP)

Pathogenesis

- Impaired cough reflex and mucociliary clearance
- Aspiration of oropharyngeal or gastric contents
- Direct extension of a contiguous infection
- Hematogenous spread from distant sites
- Inhalation of contaminated aerosols

Microbiology

- Oropharynx normally colonized with streptococci and anaerobes, but mouth of critically ill patients colonized with Gram-negative bacteria and *S. aureus*.
- Gram-negative organisms and *S. aureus* are the most common pathogens responsible for VAP. Drug-resistant organisms, such as *Pseudomonas aeruginosa, Klebsiella pneumoniae* and methicillin-resistant *S. aureus* (MRSA) also very common. Anaerobic bacteria, *Legionella* and viruses, such as herpes simplex virus, can cause VAP as well but are much less common.

Diagnosis

- No gold standard diagnostic test for VAP
- Clinical characteristics: fever, sputum production, leukocytosis, increased oxygen requirements, and a new infiltrate on chest radiograph suggestive of VAP, but not at all specific.
- Sampling of the lower respiratory tract for pathogenic organisms increases diagnostic accuracy.
 - Several methods exist: tracheal aspiration, nonbronchoscopic "mini-BALs" and fiberoptic bronchoscopy with bronchoalveolar lavage or a protected brush sampling.
 - The most accurate and cost-effective technique has yet to be determined.
- Clinical Pulmonary Infection Score (CPIS): prediction tool for diagnosis of VAP. (see Table on next page)
 - Presence or absence of fever, purulent sputum, or leukocytosis, as well as the degree of hypoxemia, character of radiographic abnormalities, and microbiologic findings.
 - Score of >6 is typically used to diagnose VAP.
 - Positive predictive value modest $-\sim60\%$ and should not be overly relied upon. More useful to ruling out VAP in patients with low score.

	Clinical Pulmonary	Infection Score	
	0 Point	1 Point	2 Points
Temperature	≥36.5 or ≤38.4	≥38.5 or ≤38.9	≥39 or <36.5
White Blood Cell Count	≥4,000 or ≤11,000	<4,000 or >11,000 Band forms ≥50 percent add 1 additional point	
Tracheal Secretions	Absence of tra- cheal secretions	Presence of non- purulent tracheal secretions	Presence of puru- lent tracheal secretions
Oxygenation	$PaO_2/FiO_2 > 240$ or ARDS		$PaO_2/FiO_2 \le 240$ and no ARDS
Chest X-ray	No infiltrate	Diffuse infiltrate	Localized infiltrate
Progression of Chest X-ray (after 48–72 hrs)	No radiographic progression		Radiographic pro- gression (if pulmo- nary edema and ARDS excluded)
Microbiology	Pathogenic bacte- ria in rare or few quantities or no growth	Pathogenic bac- teria cultured in moderate or heavy quantity Same pathogenic bacteria seen on Gram stain, add 1 additional point	

Treatment

- Treatment for VAP should begin as soon as it is suspected.
- Initial antibiotic therapy should be broad and directed at typical organisms.
- After microbiological data become available, antibiotic therapy should be tailored to specific pathogen. Patients with alternative diagnosis should have antibiotics stopped

Exposure to unnecessary antibiotics leads to colonization with drug-resistant organisms and makes future episodes of VAP more difficult to treat.

Prevention

- Avoid intubation by using non-invasive positive pressure ventilation.
- Minimize duration of mechanical ventilation by limiting sedation and performing daily spontaneous breathing trials (see Chapter 8).
- Maintain head-of-bed elevation above 30 degrees, wash hands before physical examination, and limit respiratory circuit tubing changes.
- Gastrointestinal decontamination, continual subglottic suctioning, and silver-coated endotracheal tubes promising but not yet proven.

Urinary Tract Infection

- Often cited as most common ICU infection but no consistent definition.
- Pyuria and/or bacteruria does not always indicate infection particularly in patient with indwelling urinary catheter.
- Deciding when a patient needs treatment is difficult.

- In general, antibiotic treatment should be reserved for patients at high risk of complication from untreated urinary tract infection (e.g., neutropenic or kidney transplant patients) those with possible urinary flow obstruction, recent urinary instrumentation, and those with signs or symptoms of urosepsis.
- Majority of infections caused by gram-negative bacteria (including multidrug-resistant organisms), enterococcus and candida species.
- Changing urinary catheter may transiently decrease bacteruria or candiduria but new catheter will almost always be rapidly re-colonized.

Clostridium Difficile Colitis

- Presentation
 - Most common cause of hospital-acquired infectious diarrhea
 - Clinical signs include frequent loose stools (>3 per day), fever, and abdominal pain; may also present with ileus. Some patients may have mild clinical signs and no diarrhea.
 - Recently a more rapidly progressive form of C. Diff. colitis has been seen due to a high toxin producing strain. Patients with this form may have a higher mortality and many require colectomy.
 - Leukocytosis, often extreme, frequently present
 - Typically there is recent exposure to antibiotics. Nearly all antibiotics can predispose to clostridium difficile infection but fluoroquinolones, cephalosporins and clindamycin are most often associated.
- Diagnosis: Toxin assays
 - Enzyme immuno-assay (EIA): rapid result; tests for Toxin A and B; can have false negatives
 - Stool PCR: rapid, highly sensitive and specific
 - Cytoxin assay: labor-intensive, slow, but highly specific
- Treatment
 - Non-severe disease: Metronidazole 500 mg PO/IV q8
 - Severe disease: vancomycin 125–250 mg PO q6 (higher doses sometimes used)
 - Surgery: sub-total colectomy indicated for toxic megacolon, perforation or progressive disease not likely to respond to medical therapy alone

GUIDING PRINCIPLES FOR THE USE OF ANTIBIOTICS IN THE ICU

- Severe acuity of illness often requires early broad spectrum empiric antibiotic treatment before infection identified.
- Many studies have demonstrated incrementally worsening outcomes for variety of infections with even minor delays (30 min 4 hr) of the appropriate antimicrobial treatment.
- However, low specificity of diagnostic tests (e.g., chest x-ray for the diagnosis of ventilator-associated pneumonia) often leads to overdiagnosis of infectious syndromes.
- Overuse of antibiotics leads to individual complications (e.g., colonization with resistant organisms and clostridium difficile colitis) and increased rates of antimicrobial resistance in the ICU.
- Must balance need to treat potential infections early and aggressively with harm of unnecessary antibiotics.
- It is essential to *de-escalate* antibiotic therapy as clinical situation evolves.

- Antibiotic de-escalation involves:
 - Stopping antibiotics when it is clear that no infection is present.
 - Tailoring antibiotics when sensitivity of infecting organism is known.
- Antibiotic resistance in the ICU
 - Factors leading to high rates of antimicrobial resistance in the ICU: high rates of previous exposure to broad-spectrum antibiotics; high use of invasive catheters; high rates of co-morbid conditions.
 - The most commonly encountered antibiotic resistant infections in the ICU are:
 - Methicillin-resistant S. aureus (MRSA)
 - Vancomycin-resistant Enterococcus (VRE)
 - Resistant gram-negative organisms (Pseudomonas, ESBLs, KPC-producing Klebsiella, Acinetobacter)
- Antifungal therapy in ICU
 - Candida species far and away are the most common fungal pathogen in the ICU.
 - Other fungi causing infection in the ICU include *aspergillus* sp. and zygomycoses but these occur primarily in the severely immunosuppressed with either neutropenia or T-cell dysfunction (AIDS, transplantation, high-dose steroid therapy).
 - Some patients may be at high risk of invasive fungal infection and may benefit from empiric antifungal therapy when presenting with sepsis.
- Risk factors for Candida bloodstream infection:
 - TPN, GI surgery or bowel disruption, neutropenia/hematologic malignancy/bone marrow transplant/high dose steroids, previous exposure to broad-spectrum antibiotics, high APACHE score, colonization with Candida sp. at multiple sites.

	Typical E	mpiric Antibiotic Regimens	
Catheter- Related Bloodstream Infection	Gram positive bacteria Preferred: Vancomycin Alternative: Daptomycin	Gram negative bacteria (if high risk or sepsis) Third or fourth generation cephalosporin (e.g., ceftriaxone or cefepime) or β-lactam/ β-lactamase inhibitor (e.g., piperacillin-tazobactam) or carbapenem (e.g., imipenem) And aminoglycoside (e.g., gentamicin) or fluroquinolone (e.g., ciprofloxacin)	Fungal (if high risk and sepsis) Eichinocandin (e.g., micafungin)
Ventilator- associated Pneumonia	Gram positive bacteria Vancomycin or Linezolid	Gram negative bacteria Antipseudomonal cephalosporin (e.g., cefepime or ceftazidime) or β-lactam/ β-lactamase inhibitor (e.g., piperacillintazobactam) or carbapenem (e.g., imipenem) And aminoglycoside (e.g., gentamicin) or fluroquinolone (e.g., levofloxacin)	

	Other Antibiotics	
Antibiotic	Spectrum	
Vancomycin	Gram ⊕ bacteria incl. MRSA, PCNase-producing pneumococci and enterococci (except VRE)	
Linezolid Daptomycin Quinopristin/ Dalfopristin	GPC incl. MRSA & VRE (check susceptibility for VRE)	
Quinolones	Enteric GNR & atypicals. 3rd & 4th gen. ↑ activity vs. Gram ⊕.	
Aminoglycosides	GNR. Synergy w/ cell-wall active abx (β-lactam, vanco) vs. GPC.	
Macrolides	es GPC, some respiratory Gram ⊖, atypicals	
TMP/SMX Some enteric GNR, PCP, Nocardia, Toxoplasma, most commacquired MRSA		
Clindamycin	Most Gram ⊕ (except enterococci) & anaerobes (B. fragilis resistance increasing)	
Metronidazole	Almost all anaerobic Gram ⊖, most anaerobic Gram ⊕	
Doxycycline Rickettsia, Ehrlichia, Chlamydia, Mycoplasma, Nocardia, Lyme		
Tigecycline	Many GPC incl. MRSA & VRE; some GNR incl. ESBL but not Pseudomonas or Proteus. Approved for abdominal or skin/soft tissue infections. Check susceptibility if organism isolated.	

MRSA, methicillin-resistant staphylococcus aureus; PCN, penicillin; TMP/SMX, trimetoprime + sulphonamide; GPC, gram positive cocci; GNR, gram negative rods; ESBL, extended spectrum beta lactamase.

The following tables of spectra of activity for different antibiotics are generalizations. Sensitivity data at your own institution should be used to guide therapy.

	Penicillins		
Generation	Properties	Spectrum	
Natural (e.g., penicillin)	Some GPC, GPR, GNC, most anaerobes (except <i>Bacteroides</i>)	Group A streptococci Enterococci, Listeria, Pasteurella Actinomyces, Syphilis	
Anti-Staph (e.g., nafcillin)	Active vs. PCNase-producing Staph Little activity vs. Gram ⊖	Staphylococci (except MRSA) Streptococci	
Amino (e.g., ampicillin)	Penetrate porin channel of Gram ⊖ Not stable against PCNases	E. coli, Proteus, H. influenzae Salmonella, Shigella Enterococci, Listeria	
Extended (e.g., piperacillin)	Penetrate porin channel of Gram ⊖ More resistant to PCNases	Most GNR incl. Enterobacter, Pseudomonas, Serratia	
Carbapenem (e.g., imipenem)	Resistant to most β-lactamases	Most Gram ⊕ and ⊖ bacteria including anaerobes, but <i>not</i> MRSA or VRE	
Monobactams (aztreonam)	Active vs. Gram \odot but not Gram \oplus	Gram ⊖ bacterial infxn in Pt w/ PCN or Ceph allergy	
β -lact. Inhib. (e.g., sulbactam)	Inhibit plasma-mediated β-lactamases	Adds Staph, B. fragilis and some GNR (H. influenzae, M. catarthalis, some Klebsiella); intrinsic activity aganist Acinetobacter (sulbactam only)	

	Cephalosporins	
Not active against ESBL producing GNRs or MRSA.		
Generation	Spectrum	Indications
First (e.g., cefazolin)	Most GPC (incl. Staph & Strep, not MRSA) Some GNR (incl. E. coli, Proteus, Klebsiella)	Used for surgical ppx & skin infxns
Second (e.g., cefuroxime, cefotetan)	↓ activity vs. GPC, ↑ vs. GNR. 2 subgroups: Respiratory: H. influenzae & M. catarrhalis GI/GU: ↑ activity vs. B. fragilis	PNA/COPD flare Abdominal infxns
Third (e.g., ceftriaxone)	Broad activity vs. GNR & some anaerobes Ceftazidime active vs. Pseudomonas	PNA, sepsis, meningitis
Fourth (e.g., cefepime)	↑ resistance to β-lactamases (incl. of Staph and Enterobacter)	Similar to 3rd gen. MonoRx for nonlocaliz- ing febrile neutropenia

SEPSIS AND SEPTIC SHOCK, THE SURVIVING SEPSIS GUIDELINES 2012

- Systemic Inflammatory Response Syndrome (SIRS): host response to a nonspecific insult, infectious or noninfectious.
 - Defined as ≥ 2 of the following:
 - Temperature >38°C or <36°C
 - Heart rate >90 per minute
 - Respiratory rate >20 per minute or PaCO₂ < 32 mm Hg
 - WBC > 12,000 or $<4,000/\text{mm}^3$, or >10% bands
- **Sepsis:** Infection (confirmed or suspected) + SIRS
- Severe Sepsis: sepsis associated with end-organ dysfunction or failure such as hypotension, hypoperfusion, hypoxemia, or oliguria. Tissue hypoxia may be present despite normal vital signs.
- **Septic Shock:** severe sepsis associated with hypotension and vasopressor requirement (hemodynamic instability) despite of sufficient iv fluid resuscitation (20 ml/kg of colloids or 40 ml/kg of crystalloids).

SUMMARY OF RECOMMENDATIONS FROM THE SURVIVING SEPSIS GUIDELINES 2012

(based on update presented at the 2012 Society of Critical Care Medicine meeting, Houston, TX)

The following evidence-based classification is used to grade the quality of evidence and the strength of recommendations:

Quality of evidence: A (highest), B, C, D (lowest)

Strength of recommendation: 1 (recommended), 2 (suggested)

Hospital-wide protocolized performance improvement efforts should be implemented (1C) for the management of sepsis, and performance should be measured against those.

Initial Resuscitation

Protocolized resuscitation should begin immediately once shock is diagnosed (regardless of the pt's

location) for pts in septic shock (tissue hypo-perfusion: hypotension persisting after sufficient fluid resuscitation or if blood lactate levels >4 mmol/l).

The goals of resuscitation during the first 6 hrs of management are (1C):

- Central venous pressure (CVP) 8–12 mm Hg; 12–15 if mechanically ventilated.
- Mean arterial pressure ≥65 mm Hg
- Urine output ≥ 0.5 ml/kg/hr
- Central venous (sup. vena cava) oxygen saturation ($ScvO_2$) $\geq 70\%$ or mixed venous oxygen saturation (SvO_2) ≥ 65 mm Hg.
- For pts with lactate elevation, continue fluid resuscitation until the lactate is normalized (2C) If venous O₂ saturation target not achieved (despite of achieving CVP target)
- Transfuse RBC to achieve a Hct of >30% (2C) and/or
- Administer dobutamine (up to 20 mcg/kg/min) to help achieve venous O₂ saturation target (2C)

Diagnosis

- Obtain at least 2 blood cultures (preferably before antimicrobial therapy is administered, however, antibiotic administration should not be delayed more than 45 min in order to obtain these cultures) (1C)
- Blood cultures should be obtained from peripherals veins/arteries; one may be obtained from indwelling catheters if the catheter has been in place longer than 48 hr.
- Use 1,3 beta-D-glucan assay (2B) and mannan and anti-mannan antibody assays for the early diagnosis of invasive candidiasis (2C)
- Obtain additional diagnostic imaging studies after the pt is stabilized and is safe to move.

Antibiotic Therapy

- Begin iv antibiotics as soon as possible, but no later than within 1 hr of identifying septic shock (1B) or severe sepsis (1C)
- Use broad-spectrum agents with good penetration into presumed source (double gram negative and MRSA coverage)
- Reassess antimicrobial regimen to optimize efficacy, prevent resistance, and reduce toxicity. Remember to re-evaluate daily and de-escalate as soon as culture data is available.
- Stop antibiotics if the cause of illness is non-infectious

Source Control

- Specific anatomical diagnosis (nidus) of infection should be sought (e.g. necrotizing soft tissue infection, peritonitis with intra-abdominal infection, cholangitis, intestinal infarction, etc.) or ruled out, and emergent source control be sought as rapidly as possible (*Crit Care Med.* 2008;36:296).
- Surgical drainage (if required) should be undertaken for source control within the first 12 hrs after the diagnosis (1C)

Fluid Therapy

- Crystalloids should be the primary fluid used for initial resuscitation (1A)
- Albumin can be added to initial fluid resuscitation (2B)
- Recommend against the use of hydroxyethyl starches with MW > 200 kDa (1B)
- For patients with signs of tissue hypoperfusion due to sepsis and hypovolemia a minimum of >1,000 ml crystalloids (minimum of 30 ml/kg resuscitation) should be administered within the first 4–6

hrs. More fluid maybe needed to achieve the goals of initial fluid resuscitation as described above (1B).

• For fluid challenge, recommend the administration of incremental fluid boluses to the goals described above and until hemodynamic improvement occurs in the dynamic (delta pulse pressure, stroke volume variation) or static (arterial pressure, HR) variables (1C) measures.

Vasopressor Therapy and Vasopressors

- Recommend that vasopressor therapy initially target a mean arterial BP (MAP) 65 mm Hg (1C).
- Norepineprine should be the first-line pressor used (1B)
- Epinephrine should be added (or substituted) when blood pressure is poorly responsive to norepinephrine (2B)
- Vasopressin 0.03 U/min may be added to or substitute for norepinephrine (2A)
- The use of dopamine (as an alternative to norepinephrine) is only suggested for highly selected patients at very low risk of arrhythmias, with low cardiac output and low HR (2C)

Inotropic Therapy

- Dobutamine should be administered (or added to vasopressors) when the following are present (1C):
 - Myocardial dysfunction (elevated cardiac filling pressures with low cardiac output)
 - Ongoing signs of tissue hypoperfusion despite of achieving adequate intravascular volume and mean arterial pressure

Blood Product Administration

• Transfuse RBCs to maintain Hgb > 7.0 g/dl once hypoperfusion is resolved, and there are no signs of myocardial ischemia or severe other heart disease, severe hypoxemia, acute hemorrhage or lactic acidosis (for those keep Hct > 30, Hgb > 10 g/dl) (1B).

Mechanical Ventilation, Sepsis-Induced ARDS

- Recommend using 6 ml/kg tidal volumes for patients with ARDS/ALI or at risk of ARDS (some exceptions are acceptable based on pt respiratory drive) (1A), and to maintain plateau pressures of ≤30 cm H₂O (in patients with normal extra-pulmonary compliance) (1B).
- Higher levels of positive end-expiratory pressure (PEEP) should be used when higher FiO₂ is required for pts with more severe ARDS (2C)
- May use recruitment maneuvers for pts with severe refractory hypoxemia (2C)
- Suggest prone positioning for pts with very severe ARDS $PaO_2/FiO_2 < 100$ even after recruitment maneuvers have been performed (2C)

Sedation, Analgesia, and Neuromuscular Blockade in Sepsis

- Neuromuscular blocking agents (NMBA) should be avoided for patients without ARDS, as there is a risk a prolonged blockade.
- If NMBA are used, intermittent small boluses or low dose infusion should be used, with monitoring of the depth of the blockade (with a train-of-four nerve stimulator) (1C)
- For patients with severe sepsis-induced ARDS a short course (no more than 48 hr) of NMBA can be used (2C) while monitoring blockade.
- Appropriate sedation and pain control have to be maintained while the patients receive NMBA.

Glucose Control

- Begin insulin when 2 consecutive blood glucose measurements exceed 180 mg/dl
- A protocolized glucose management strategy should aim to keep the higher level of blood glucose < 180 mg/dl (1A)

Deep Venous Thrombosis (DVT) Prophylaxis

- Recommend the use of daily sc low molecular weight heparin (LMWH) for the prevention of DVT (1B)
- If LMWH is not available (or deemed too high risk for bleeding) low dose sc un-fractionated heparin should be used (1B)
- Recommend the combination of heparin pharmacotherapy and pneumatic compression devices (unless contraindicated) for pts with severe sepsis. (2C)

Nutrition

• Early appropriate nutritional support should begin as soon as it is safe. The enteric route is preferred, unless contraindicated.

Corticosteroids

- Recommend NOT using corticosteroid treatment for adult septic shock patients if fluid resuscitation and vasopressor therapy are able to restore tissue perfusion and hemodynamic stability (no mortality benefit (*N Engl J Med.* 2008;358:111)).
- When tissue perfusion is impaired and hemodynamics are unstable, 200 mg iv hydrocortisone can be given in continuous infusion (2C).
- Recommend NOT using ACTH stimulation test (2B).
- Pts with septic shock should receive hydrocortisone rather than other steroids (2B).
- For steroids hydrocortisone ALONE should be used without fludrocortisones (1B)

Goals of Care, Communication of Prognosis

- Discuss with patients and families the:
 - Goals of care, and the prognosis for achieving those goals (1B)
 - Integrate those goals into one unified treatment plan, including palliative care plans and end-of-life planning (1B)
 - Goals of care should be addressed as early as possible but no later than 72 hrs after admission depending on cultural considerations (2C)

SEVERE ACUTE PANCREATITIS

- Most common causes: alcohol, biliary stones, drugs, hypertriglyceridemia, infection.
- Diagnosis: clinical and laboratory features
 - Constant epigastric pain radiating to the back
 - Nausea and vomiting
 - Flank (Grey-Turner's sign) or umbilical (Cullen's sign) ecchymoses
 - Elevated amylase and lipase (more specific), levels do not correlate with severity
- Severity determination: early detection may be difficult

Ranson's Criteria: Severe Pancreatitis is Likely if the Score ≥3 (Surg Gynecol Obstet. 1976;143:209)

- At admission (1 point each):
- Age $> 55 \text{ yr} \cdot \text{AST} > 250 \text{ IU/l} \cdot \text{LDH} > 350 \text{ IU/l}$
- WBC $> 16,000 \text{ cells/mm}^3$ Glucose > 200 mg/dl

At 48 hrs (1 point each):

- Ca < 8 mg/dl Hct \downarrow > 10% PaO₂ < 60 mm Hg
- Base deficit >4 mEq/l Fluid sequestration >6 l
- BUN increase ≥5 mg/dl following IVF
 - Organ failure, hypotension or Apache II ≥ 8
- CT criteria: <72 hr from disease onset may underestimate pancreatic necrosis
 - Single or multiple fluid collections (*Radiology*. 1990;174:331)
 - Necrosis, abscess, pseudocyst
 - EPIC (extrapancreatic inflammation on CT) score ≥4 (*Pancreas*. 2007;34:185–190)
 - Presence of pleural effusion(s), ascites, and retroperitoneal fluid collection(s), mesenteric inflammation

• Treatment:

- Vigorous fluid resuscitation: 200–350 ml/hr for 48 hr if cardiac status permits
- Supplemental oxygen, correction of metabolic abnormalities
- Antibiotics for sepsis, infected necrosis/abscess; no prophylactic antibiotics indicated. Sterile vs. infected necrosis determined by percutaneous aspiration
- Nutrition: oral intake as tolerated (usually in the absence of significant nausea, vomiting or pain). When nutrition support needed enteral route preferred. TPN for intolerant patients who remain NPO > 7 d.
- Analgesia: frequently require parenteral narcotics
- ERCP: gallstone pancreatitis, cholangitis
- Surgery:
 - For infected pancreatic necrosis, timing dependent on surgeon.
 - For abscess (may also be treated via percutaneous drainage)
 - Cholecystectomy for gallstone pancreatitis

ENDOCRINE AND RENAL ISSUES

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ENDOCRINE DISORDERS IN THE ICU

Hyperglycemia – Diabetic Emergencies

- Diabetic Ketoacidosis (DKA)
 - Precipitating Factors five I's
 - Insulin nonadherence
 - Infection/inflammation
 - Ischemia/Infarction
 - Intra-abdominal process pancreatitis, cholecystitis, appendicitis, splenic injury, ischemic bowel
 - Iatrogenesis steroids
 - Manifestations
 - Altered mental status
 - Nausea, vomiting, abdominal pain
 - Volume depletion
 - Kussmaul breathing
 - Acetone odor on breath
 - Polyuria/polydypsia
 - Volume depletion (and polyuria) less likely in ESRD
 - Test
 - Check serum and urine glucose, acetone, beta-hydroxybutyrate
 - Management
 - Insulin infusion until AG (anion gap) closed
 - 10 units IV push \rightarrow 0.1 units/kg/hr
 - Once glucose <250 and AG closed transition to SQ insulin with IV overlap 2–3 hrs
 - If glucose <250 and AG still high, continue insulin infusion and add dextrose infusion
 - Volume resuscitation patients are profoundly volume depleted from polyuria
 - Start NS 10–14 ml/kg/hr depending on degree of volume depletion and cardiac function
 - Need to monitor closely for resultant hypernatremia after volume resuscitation
 - Electrolytes
 - Sodium pseudohyponatremia
 - Corrected Na = Measured serum Na + $1.6 \times (glucose-100)$
 - May in fact be hypernatremic from osmotic diuresis
 - Potassium total body K is depleted; serum K may be artificially high due to volume depletion and acidosis; with volume resuscitation and correction of acidosis true K depletion will become apparent
 - If K < 4.5 add 20–40 meq KCl to IVF
 - Bicarbonate

- If pH < 7.0, can substitute isotonic bicarbonate for initial fluid resuscitation
- May need to increase threshold for K supplementation (e.g., <5.3) due to intracellular shift from correcting acidosis
- Phosphate often total body PO₄ depleted; like K depletion, may be masked by volume depletion and acidosis and revealed/magnified by volume resuscitation and correction of acidosis
 - Administer phosphate if < 1.0
- Hyperglycemic Hyperosmolar Nonketotic (HHNK) Coma
 - Precipitating Factors
 - Same as DKA
 - Manifestations
 - Altered mental status
 - Volume depletion
 - Polyuria/polydypsia
 - Management
 - Insulin lower doses than in DKA, egs 0.05 units/kg/hr
 - Volume resuscitation may also be profoundly free water depleted
 - Start NS or ½ NS 10–14 ml/kg/hr depending on degree of volume depletion, free water depletion, and cardiac function

Glycemic Control

- Non-diabetics
 - No mortality benefit from intensive insulin therapy (generally glucose of 80–110 mg/dl) in several studies of both surgical and medical patients and in fact intensive control may increase mortality (*NEJM.* 345;1359, *NEJM.* 354;449, *NEJM.* 360;1283)
 - Less intensive arm generally 140–180 mg/dl; therefore suggest goal of blood glucose <180 mg/dl
- Diabetics
 - Subanalyses of diabetics or dedicated diabetic trials did not show a mortality benefit from intensive insulin therapy, including in setting of acute MI; therefore suggested goal of blood glucose <180 mg/dl (*Diabetes Care.* 32;1119)

Adrenal Insufficiency

- Absolute Adrenal Insufficiency
 - Primary AI should receive usual dose and possibly increased dose of corticosteroid if critically ill or undergoing major surgery
 - 100–150 mg intravenous hydrocortisone or 50–100 mg hydrocortisone q6–8 hrs peri-procedure or during critical illness may be reasonable (*JAMA*. 287;236)
- Relative Adrenal Insufficiency in Sepsis (JAMA. 288;862; see Chapter 10 for sepsis)
 - Criteria
 - Severe hypotension refractory to volume resuscitation and at least one vasopressor
 - Treatment
 - Hydrocortisone 50–100 mg q6–8 hrs

Thyroid Disease

• Hypothyroidism

- Definition
 - Low free T4
 - TSH variable (primary-low; secondary (central)-variable)
- Clinical Manifestations
 - General
 - Metabolic slowing weakness, fatigue, cold intolerance, weight gain, delayed relaxation of DTRs
 - Accumulation of matrix substances (glycosaminoglycans) dry skin, non-pitting edema
 - Other depression, dysmenorrhea
 - Subclinical Hypothyroidism
 - Mildly elevated TSH with normal T4
 - Euthyroid Sick Syndrome
 - Abnormal TFTs in setting of non-thyroidal illness (critical illness, post-CABG)
 - Low T4, low T3, high TSH
 - Reverse T3 may be high
 - No benefit to thyroid hormone replacement
 - Myxedema Coma
 - Myxedema with hypotension, hypothermia, hyponatremia
- Etiology and Precipitants
 - With goiter Hashimoto's, post-thyroiditis, Iodine deficiency; general risk factors include age, female sex
 - Without goiter Surgical removal or destruction, neck radiation exposure, radioactive iodine, amiodarone
- Management
 - General levothyroxine replacement at 1.5–1.7 mcg/kg/d, may convert to IV if unable to take PO
 - Myexedema coma 5–8 mcg/kg of T4 IV then 50–100 mcg IV daily; may also need glucocorticoid replacement for concomitant adrenal insufficiency
- Hyperthyroidism
 - Definition
 - Elevated free T4 and free T3
 - TSH low unless TSH-secreting tumor
 - Clinical Manifestations
 - General
 - Restlessness, tachycardia, AFib, weight loss, hyperreflexia, dysmenorrhea, fine hair
 - Thyroid Storm
 - Tachycardia, delirium, hyperthermia, systolic hypertension, GI symptoms
 - Etiology and Precipitants
 - Graves' disease, thyroiditis, toxic adenomas, TSH-secreting pituitary tumors, iodine-induced
 - Acute illness, infection, post-partum
 - Management ICU focus
 - Thyroid Storm
 - Beta blockers for tachycardia, especially propranolol (decreases T4 to T3 conversion)
 - PTU
 - Iodide (for "Wolff-Chaikoff" effect iodine administration temporarily inhibits iodine

organification in the thyroid gland)

• Steroids (decreases T4 to T3 conversion)

Hypopituitarism

- Manifestations
 - Central adrenal insufficiency (ACTH deficiency) with mineralocorticoid axis intact
 - Central hypothyroidism (TSH deficiency) need to follow T4 directly as TSH may be low (or inappropriately normal)
 - Central Diabetes Insipidus (ADH deficiency) polyuria, mild hypernatremia
 - Other abnormalities prolactin deficiency, growth hormone deficiency, FSH and LH deficiency
- Etiologies
 - Post transphenoidal surgery, trauma, tumor, infection, infiltration (sarcoid, hemochromatosis), Sheehan's syndrome (ischemia), cavernous sinus thrombosis, pituitary apoplexy (hemorrhage)
- Management
 - See individual conditions

RENAL ISSUES ENCOUNTERED IN THE ICU

Acute Kidney Injury – the most commonly seen renal problem in the ICU Definitions – largely for epidemiologic/research purposes – RIFLE (*Crit Care*. 8;R204) and AKIN (*Crit Care*. 11:R31); from AKIN:

- Serum Cr rise abrupt (within 48 hrs) absolute increase in SeCr of 0.3 mg/dl or ≥50%
- Oliguria < 0.5 ml/kg for 6 hrs

Etiology

- Prerenal decreased perfusion
 - Causes:
 - Volume depletion absolute or third spacing (↓ ECV)
 - Hypotension (even relative) from ↓ CO or ↓ SVR
 - Renal vasoconstriction (NSAIDs, ACE/ARB, CNIs, hepatorenal syndrome, hypercalcemia)
 - Hepatorenal Syndrome (HRS)
 - Definitions/Diagnosis
 - Type I (days to 2 wks) vs. Type II (weeks to months)
 - \bullet Usually bland sediment, UNa usually <10
 - No response to volume resuscitation
 - No other cause volume depletion (recent paracentesis), infection (especially SBP), hypotension/shock, nephrotoxins
 - Management
 - Colloid to increase MAP
 - Midodrine/octreotide (*Hepatol*. 29;1690)
 - Vasopressin (*NDT*. 20;1813)
 - TIPS procedure (*Gut.* 47;288)
 - Liver transplant
 - Renal Replacement Therapy (RRT) supportive if TIPS or Liver Transplant possible

- Acute Tubular Necrosis (ATN)
 - Causes:
 - Ischemic decreased perfusion, acute or as consequence of prolonged prerenal
 - Nephrotoxic drugs (AG, vancomycin, platins, amphotericin)
 - Radiocontrast Nephropathy (RCN)
 - Causes prerenal/ischemic ATN (afferent vasoconstriction), nephrotoxic ATN (oxidative damage)
 - Cr rise 24–96 hrs post-contrast
 - Prevention includes pre/post hydration, NAC 600-1,200 mg BID day prior and day of contrast
 - Pigment nephropathy myoglobin (rhabdomyolysis), hemoglobin (intravascular hemolysis)
 - Rhabdomyolysis causes prerenal/ischemic ATN (volume loss, third spacing to damaged tissue), nephrotoxic ATN (oxidative damage from myoglobin), and tubular obstruction from precipitation of myoglobin
 - Diagnosis includes urine dip positive for blood but no RBC on microscopy, elevated CK (usually >1000 IU/l)
 - Management includes volume resuscitation with NS, maintenance of high urine output with volume alone or with diuretic (lasix or mannitol) +/- alkalinization
 - Intravascular hemolysis post thrombectomy (egs DVT treatment)
 - Management same as rhabdomylysis
- Acute Interstitial Nephritis (AIN)
 - Culprits
 - Antibiotics (penicillins, sulfa, cephalosporins), NSAIDs, antacids (H2 blockers and PPIs), cancer biologics
 - Sarcoidosis, Sjogren's
 - History/Time course
 - With drug-related requires 5–7 days of previous exposure prior to manifestations (or past exposure leading to accelerated time-course on re-challenge)
 - Diagnosis based on history; sediment with WBC or WBC casts suggestive but often bland; unclear utility of urine eosinophils
 - Management
 - Removal of offending agent
 - Steroids limited evidence to support, balance with risk (especially infectious when antibiotic induced); suggested doses include prednisone 1 mg/kg (max 60 mg) for 3–14 days then taper or in severe cases pulse methyprednisolone (0.5–1 mg daily for 3 days) followed by taper
- RPGN (rapidly progressive glomerulonephritis) ICU focus
 - Etiology
 - Pulmonary-Renal Syndromes
 - ANCA
 - Anti-GBM
 - SLE-related
 - When to suspect/Clinical Manifestations
 - History suggestive (hemoptysis, SLE-related serositis)
 - Sediment with acanthocytes or RBC casts
 - Workup
 - Serology ANCA, anti-GBM, C3, C4, CH50, ANA/dsDNA

- Renal biopsy
- Management empirically while awaiting biopsy
 - Steroids 0.5–1.0 g methylprednisolone daily for 3 days, then taper
 - Induction once confirmed by biopsy, cyclophosphamide or mycophenolate depending on etiology
 - Pheresis (TPE) to be considered especially in anti-GBM if need for RRT
 - RRT for usual indications (uremia, acidosis, volume overload)
- Obstruction
 - Consider: Elderly male, recent foley catheter, history of prostate disease (BPH or cancer), abdominal/pelvic tumor (extrinsic compression), significant ascites or abdominal distension
 - Check Post Void Residual, renal ultrasound
 - Caution: Especially in setting of volume depletion, degree (or presence) of hydronephrosis may not reflect degree (or presence) of obstruction
 - Abdominal Compartment Syndrome
 - Ascites (liver failure, malignant), intra-abdominal hemorrhage (trauma, post-operative)
 - Transduce bladder pressure; 20–30 abnormally high, >30 very concerning
- Other
 - TTP-HUS (Thrombotic Thrombocytopenic Purpura and Hemolytic Uremic Syndrome)
 - MAHA (microangiopathic hemolytic anemia) and AKI (acute kidney injury); may also include other signs/symptoms fever, altered mental status
 - Associated with drugs (calcineurin inhibitor), SLE, cancers, infection, ADAMTS13 deficiency
 - Consider pheresis/TPE in addition to usual AKI management
 - Tumor lysis obstructive urate nephropathy in setting malignancy
 - Spontaneous or peri-chemotherapy
 - Usually leukemia or lymphoma, rarely solid tumors
 - Management
 - Volume expansion and maintenance of high urine output (150–300 ml/hr) +/- alkalinization
 - Allopurinol
 - Uricase administration

General Workup for Renal Problems Occurring in the ICU

- Careful history and physical exam
 - Review of vital signs/op-reports for hypotensive episodes
 - Review of medications and lab data for precipitants (e.g., ACE/ARB, NSAIDs, drop in hemoglobin/hematocrit)
 - Charting/graphing of Cr to narrow timing of insult
- FENa < 1% suggests prerenal; >2% suggests ATN; 1–2% indeterminate (Am J Med. 77;699)
- If on diuretics, FEUrea < 35% suggests prerenal; >35% suggests ATN (KI. 62;2223)
- Urine osmolality may suggest severity of ischemic ATN (the closer to isotonic, the less remaining concentrating ability and the more severe the ATN; also less likely volume sensitive/prerenal component)
- Urine microscopy and sediment analysis
- Rule out obstruction via renal ultrasound or other modality
- Further laboratory testing (serologies etc) as suggested by above evaluation

Treatment Approach/Strategies – EBM

- Failed Therapeutic Interventions
 - Diuretics (*BMJ*. 333;420)
 - Dopamine (*Lancet*. 356;2139)
 - ANP (atrial natriuretic peptide) (*NEJM*. 336;828)
 - Fenoldopam (*AJKD*. 46;26)
 - IGF-1 (KI. 55;2423)
 - Thyroxine (*KI*. 57;293)
- Hemodynamic Support
 - Maintain MAP > 65; 70–80 for optimal renal perfusion
- Volume Management
 - Judicious IVF to achieve/maintain euvolemia
 - Central venous monitoring may be helpful
- Withdrawal of offending agents
- Avoidance of nephrotoxins
 - ACE-I/ARB
 - NSAIDs
 - Contrast Dye
 - Aminoglycosides, cisplatin
- Drug Dosing/Changes
 - Assume CrCl < 10 if creatinine rising or anuric for purpose of med dosing
 - Antibiotic dosing by levels when appropriate
- Nutrition and Electrolyte Considerations
 - Minimize potassium intake
 - Minimize phosphate intake, may consider phosphate binders such as calcium acetate, sevelamer, lanthanum if taking PO; use limited (6–8 doses) aluminum hydroxide if not taking PO (will still bind salivary PO₄)
 - Reduce dietary protein (discontinue supplements) to minimize catabolism and high urea
 - Consider sodium bicarbonate PO or IV

Renal Replacement Therapy

- Indications
 - A.E.I.O.U.
 - A acidosis
 - E electrolyte abnormalities (K, Ca)
 - I ingestions
 - O overload (volume management)
 - U uremia (mental status changes, pericarditis; intractable uremic bleeding?)
- Modalities
 - Continuous vs. Intermittent: No benefit to continuous over intermittent therapy in patients with MODS (*Lancet.* 368;379)
 - Standard vs. Intensive: No benefit to intensive therapy when defined as hemodialysis 3 vs. 6 times per week or more intensive CVVH (*VA/NIH Network Trial: NEJM.* 359;7)

Continuous

- CVVH (and CVVHD/CVVHDF):
 - Driving Force: Convection/ultrafiltration water ultrafiltered across semipermeable membrane; solute dragged across and removed as well
 - Replacement Solution: Solute concentrations (Na, Cl, Buffer bicarbonate or citrate, Mg) similar to normal plasma; can include K and Ca at various concentrations
 - Anticoagulation
 - Heparin regional or systemic
 - Citrate regional or systemic (citrate used as buffer)
 - Access: Central venous catheter
 - Clinical Considerations
 - Hyperkalemia: Control of potassium is slow with continuous modalities; favor hemodialysis when hyperkalemia is of concern
 - Calcium/Phosphate: May require repletion of Ca continuously and phosphate intermittently
 - Intravascular volume control better, can change removal goals on minute-to-minute basis
 - Hemodynamics already hypotensive patients better tolerate continuous therapy, may have less risk of hypotension

Intermittent

- Intermittent Hemodialysis (IHD)
 - Driving Force: Diffusion diffusion of water (osmosis) and solute down concentration gradient across semi-permeable membrane
 - Replacement Solution (Dialysate): Sodium, Chloride, Bicarbonate near normal plasma levels, K and Ca depending on clinical scenario
 - Anticoagulation: None, heparin, or other (egs argatroban in HIT)
 - Access: Central venous catheter; Arteriovenous fistula or graft
 - Clinical Considerations: Preferred for hyperkalemia as removal is faster; Volume management harder given intermittent nature; Hemodynamics can be limiting if baseline hypotension, both for volume removal and successful treatment in general
- SLED (slow low-efficiency dialysis) and SCUF (slow continuous ultrafiltration)
 - Dialysis or ultrafiltration at low blood flow to minimize hypotension; not available at all centers
- Peritoneal Dialysis
 - Driving Force: Diffusion diffusion of water (by osmosis) and solute down concentration gradient across semi-permeable membrane the peritoneum
 - Replacement Solution (dialysate): Na, Cl, Bicarbonate near normal plasma levels; glucose is solute determining gradient for osmosis, concentration can be varied to remove more or less volume
 - Access: Peritoneal catheter; temporary catheter can also be placed acutely at some centers
 - Clinical Considerations: Acute PD possible though not available at all centers due to inability to place catheters acutely or other staffing limitations

Special Considerations

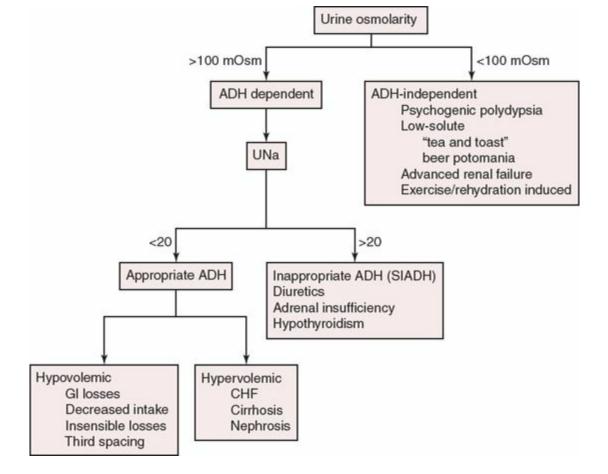
- Control of Intra-Vascular Volume
 - ALI/ARDS in patients without need for RRT, conservative fluid management may decrease time on ventilator and time in ICU though no significant affect on mortality (*NEJM*. 354;2564); unclear how this applies to patients requiring RRT
- Acidemia

- Lactic Acidosis RRT will remove small amount of lactate and provide added buffer; however underlying cause of lactic acidosis must be addressed
- Toxins and Ingestions consult nephrology early
 - Lithium
 - Altered mental status, tremor, level >2
 - Toxic Alcohols
 - Calcium oxalate crystals may be present with ethylene glycol
 - Ethanol or fomepizole antagonize metabolism and may prevent toxicity while awaiting dialytic therapy
 - Salicylates
- Additional Issues:
 - Increased ICP (with liver failure, intra-cerebral hemorrhage, or CVA) when requiring RRT, may favor slower removal/equilibration characteristic of continuous modality to avoid worsened cerebral edema

ELECTROLYTE ABNORMALITIES MOST COMMONLY ASSOCIATED WITH RENAL DYSFUNCTION

- Hyperkalemia (see Chapters 1 and 6)
- Hyponatremia
 - Definition: Represents total body water overload
 - Symptoms altered mental status, gait instability, seizure, coma
 - Etiology and forms of hyponatremia
 - Appropriate ADH: decreased EAV (hypovolemia, hemorrhage, third-spacing, CHF, cirrhosis, nephrosis, myxedema, cortisol deficiency)
 - Inappropriate ADH
 - Central
 - Intracranial process CVA, ICH, tumor, infection
 - Medications antidepressants, antipsychotics
 - Other pain, post-op (especially orthopedic procedures)
 - Peripheral
 - Pulmonary process SCLC, PNA, ILD, PPV, PTX, asthma/COPD
 - Exogenous
 - Oxytocin
 - DDAVP (iatrogenic for panhypopit)
 - ADH-independent polydypsia, decreased solute intake ("tea and toast," beer potomania), altered renal function, exercise-induced
 - Other pseudohyponatremia, generally lab artifact in setting hyperglycemia, hyperlipidemia, hyperproteinemia (egs paraprotein disease)
 - Workup
 - Urine osm, Urine Na
 - History and physical for volume status

Figure 1. Differential Diagnosis of Hyponatremia



- Management (Caution: Maximum rate of correction should not exceed 3 mEq/hr to avoid central pontine myelinolysis)
 - Remove ADH stimulus
 - Treat underlying cause (ICH, PNA)
 - Volume repletion
 - Re-compensate heart failure
 - d/c causative meds
 - Free water restriction
 - Increase osmole intake (salt tabs, urea infusion)
 - Normal saline +/- loop diuretic
 - NS only helpful if Uosm < NSosm (308); caution in SIADH unless administering diuretic concomitantly to lower urine osm
 - Loop diuretic destroys medullary concentrating gradient, decreasing the osmotic gradient for H2O reabsorption, thereby decreasing ADH responsiveness
 - Hypertonic saline
 - Use if symptomatic or if free water restriction fails to correct
 - Estimate initial hourly rate as sodium required to increase SeNa by 8–12 meq/l in first 24 hrs: $[NaDeficit/513] \times [1,000 \text{ ml}/24 \text{ hrs}]$

where NaDeficit = $8 \times \text{TBW}$ (for goal 8 meq/l in 24 hrs) where TBW = $(0.60 \times \text{Wt in kg}) \times 0.85$ if female $\times 0.85$ if elderly

- Value should always be <60 ml/hr (use online calculator to confirm rate)
- Recheck SeNa very frequently as adjustment will be needed
- Demeclocycline
- Aquaporin channel blockers ("aquaretics" tolvaptan, conivaptan)
- Special Considerations

- In adrenal insufficiency
 - Administration of steroids in this setting can lead to rapid diuresis and result in overly rapid correction of Na; requires frequent monitoring and possible need for free water or ADH administration to slow rate of correction
- Hypokalemia
 - Caution when repleting potassium in setting of hyponatremia as rapid repletion can lead to cellular shift of Na out of cells, exaggerating/accelerating Na rise
- Hypernatremia
 - Definition: Total body free water deficient
 - Etiology
 - Insensible losses/GI losses in setting of inadequate access to free water
 - Osmotic diuresis (egs DKA)
- Diabetes insipidus (DI) as the cause of hypernatremia
 - Central
 - Nephrogenic
 - Drugs Li, amphotericin, ifosfamide
 - Metabolic hypercalcemia, severe hypokalemia
 - TI disease sarcoid, SCD, Sjogren's
- Workup
 - History and physical for volume status, source of loss
 - Urine Osm and urine Na
 - UOsm > 600 and UNa < 20 suggests extrarenal loss, UNa > 20 suggests renal loss
 - If DI suspected: Uosm < 300 suggests complete, 300–600 suggests partial
 - Management
 - Correct underlying cause (restore euvolemia, manage DKA)
 - Replenish free water deficit
 - Target decreasing Na no more than 0.5 meg/l/hr to avoid cerebral edema
 - Calculate free water deficit to replete in first 24 hrs as:
 - Free water deficit = desired change in SeNa \times TBW = 8–12 \times TBW where TBW = 0.60 \times Wt in kg, 0.50 \times Wt in kg if female if elderly use 0.50 for men and 0.45 for women
 - Divide by 24 and replace hourly via IV infusion of D5W or enterally via diluted TF or intermittently as free water boluses
 - Also need to take into account and match ongoing losses to ensure net repletion of free water deficit
- Diabetes Insipidus (DI)
 - Central DI
 - Treat with DDAVP
 - Nephrogenic DI
 - Treat underlying cause if feasible
 - Salt and protein restrict (decreased osmolar intake obligates less free water loss)
 - Distal diuretics (induces mild volume depletion which leads to greater proximal reabsorption of filtrate and less delivery distally preventing free water loss
 - NSAIDs prostaglandin inhibition eliminates prostaglandin-induced antagonism of ADH
- Special Considerations
 - For increased ICP mild hypernatremia may be desirable to decrease cerebral edema

ISSUES RELATED TO OSMOLALITY AND OSMOREGULATION

- Serum Osmolality is calculated with the following formula: $2 \times \text{Na} + (\text{blood glucose/18}) + (\text{BUN/2.8})$
- In ethanol intoxication, add EtOH/4.6
- Normal plasma range is 275 to 295 mosmol/kg
- It is an important factor to consider in clinical conditions where access to water is limited, as can be seen in critical illness.
- Thirst and normal kidneys will compensate for changes in urine osmolality in healthy individuals with the influence of volume-receptors and osmo-receptors. Physiologically, maintenance of plasma volume generally takes precedence over osmolality
- Plasma hyperosmolality with urine hypo-osmolality is a marker of diabetes insipidus (central or nephrogenic)
- Plasma hypoosmolality with concentrated urines is a marker of either appropriate (prioritizing maintenance of circulating volume) or inappropriate ADH secretion

The abnormalities of calcium, magnesium and phosphate homeostasis and their etiology, workup and management are discussed in details in Chapter 8.

SCORING SYSTEMS FOR THE SEVERITY OF ILLNESS

EDWARD KELLY, MD

Scoring systems have been devised to describe severity of illness and to predict the morbidity and mortality of critically ill patient populations. Several have been proposed for general use in non-selected ICU populations. APACHE, SAPS, and SOFA gained the most widespread use. Each scoring system is based on retrospective analysis of large populations of ICU patients using multivariate linear regression or other statistical tools, to identify physiologic markers of severity of illness that correlate with incidence of complications and mortality. The degree of correlation is then used to weight the most reliable parameters and construct a numerical score that correlates with complications and mortality better than any individual parameter.

Acute Physiology and Chronic Health Evaluation (APACHE) (Crit Care Med. 1985;13:818)

- Began as an index of severity of disease accounting for 12 variables and using weighted multipliers to give a score of 0–71; 71 indicates most severe disease
- Renal function, age, Hct, Na, K, oxygenation, Temp, HR, RR, WBC, GCS, immune suppression
- APACHE II system published in 1985 is in the public domain
- There are many online resources to calculate APACHE II score (http://www.mdcalc.com/apache-ii-score-for-icu-mortality)
- APACHE III is proprietary, has better accuracy, is based on more robust retrospective dataset and weighs variables differently
- Designed to be calculated within the first 24 hrs of ICU admission, and not repeated

Simplified Acute Physiology Score (SAPS) (JAMA. 1993;270:2957)

- An index of severity of disease accounting for 17 variables and using weighted multipliers to give a score of 0–163; 163 indicates most severe disease
- Variables similar to APACHE II, but also include total bilirubin, BUN, type of ICU admission (urgent, emergent, or re-admission), serum bicarbonate, and systolic BP
- Based on large multicenter retrospective dataset, excludes burns, coronary disease and cardiac surgery patients
- Designed to be calculated within the first 24 hrs of ICU admission, and not repeated
- SAPS II system published in 1993 is in the public domain
- There are many online calculators (http://www.sfar.org/scores2/saps2.html)
- SAPS III was developed in 2005 in an effort to improve prognostic value and to reflect changes in expected complication rate on the basis of new therapies. Prognostication using the SAPS III system requires calibration of the target patient group's data variables with a reference group within the SAPS II cohort

Sequential Organ Failure Assessment (SOFA) (Intensive Care Med. 1996;22:707)

- Devised as a daily score, unlike APACHE and SAPS
- Grades degree of impairment for 6 vital organ systems: Respiratory, Renal, Coagulation, Hepatic, Cardiovascular, and Central Nervous system

- Impairment graded as 1–4, 4 being most severe organ failure
- Overall score ranges from 6–24, with no zero; a score of 24 indicates greatest burden of organ failure
- Descriptive only, no calculations involved for predicted mortality
- SOFA system published in 1996 is in the public domain
- Many online calculators (http://www.mdcalc.com/sequential-organ-failure-assessment-sofa-score)

No currently available system allows prediction of mortality for unselected patients, but the 3 systems in common use do facilitate comparison of risk-adjusted morbidity and mortality rates among ICUs.

All of the ICU severity scoring systems both underestimate and overestimate mortality when used to predict outcome for an individual patient. The inaccuracy arises from the model's inability to predict certain adverse events, as well as the inability to account for potentially lethal conditions that do not manifest as organ failure until late in the course.

Several scoring systems are available for predicting highly selected individual patients' surgical mortality, based on comorbidities and procedural variables. These systems are highly specific and do not generalize to the rest of the ICU population.

Examples include the MELD score, the STS Risk Calculator for cardiac surgery patients, and the Revised Trauma Score.

Model for End-Stage Liver Disease (MELD) (Hepatology. 2000;31:864)

- Devised as a scoring system for severity of liver failure and validated to predict mortality following the Transjugular Intrahepatic Portosystemic Shunt (TIPS) procedure
- Calculates degree of hepatic impairment using three variables: serum bilirubin, serum creatinine and international normalized ratio (INR) in a weighted index. See (http://www.mayoclinic.org/meld/mayomodel7.html)
- Later adopted by the United Network for Organ Sharing (UNOS) to predict mortality rate for hepatic transplantation (*Gastroenterology*. 2003;124:91). MELD score, UNOS modification: (http://www.mayoclinic.org/meld/mayomodel6.html)

STS Risk Calculator

- Proprietary, based on the Society for Thoracic Surgery National Database (*Ann Thorac Surg.* 1997;63:903). See (*http://riskcalc.sts.org/STSWebRiskCalc273/*)
- Software calculators available only from certified vendors
- Applied pre-operatively to predict surgical outcomes
- Includes parameters of renal, neurologic, cardiac, vascular, and pulmonary function, as well as comorbidities, such as diabetes mellitus and hypertension
- Also includes type of operation, and whether urgent or emergent
- Calculates expected mortality, and rates of specific complications including wound infection, stroke, renal failure, prolonged hospital stay, and need for re-operation
- Well validated in prospective studies and used for national and state-wide quality improvement initiatives

Revised Trauma Score

- Devised (*Crit Care Med.* 1981;9:672) in 1981 as a system to grade severity of traumatic injury based on physiologic response and revised (*J Trauma.* 1989;29:623) in 1989 to a simple set of observations easily used in the field
- Public domain, in widespread use in the field and in the ICU
- Validated in numerous subsequent prospective trials

ICU scoring systems are frequently utilized for resource allocation and cost effectiveness policy making. (*Intensive Care Med.* 2007;33:1329) Physiologically based scoring systems also enable suitable comparison of outcomes from one ICU to another, and facilitate study of new treatments, clinical effectiveness measures, and quality assurance and patient safety initiatives.

PREVENTIVE STRATEGIES AND EVIDENCE-BASED PRACTICE

SHANNON S. MCKENNA, MD

Research over the last 10–15 yrs has identified effective ways to prevent many of the common sequelae of critical illness. The challenge for all institutions is to effectively and universally implement evidence-based care improvement practices. This requires commitment and team work across multiple disciplines.

CENTRAL VENOUS CATHETER (CVC) ASSOCIATED BLOOD STREAM INFECTIONS (CABSI)

Epidemiology (NEJM. 2006;355:2725)

- 80,000 infections/year; 28,000 deaths/year
- >\$2 billion annual cost
- Preventable

General Principles for an Effective CABSI Prevention Program (*Infect Control Hosp Epidemiol.* 2008;29:S22)

- Must be institutional priority at leadership level
- Institution wide, standardized education (indications for CVC use, proper sterile technique for placement, site maintenance, hub access techniques) for all personnel placing, maintaining or utilizing CVCs
- Checklist used during catheter insertion (see below) to assure proper sterility
- All essential supplies located in one location on a given unit
- Infection rate monitored and data regularly reviewed by ICU and hospital leadership

Insertion

- Avoid femoral site (some data favor subclavian over internal jugular)
- Use checklist in real time to assure maintenance of sterility
- Observer executing checklist must be empowered to stop procedure for violations

Essential Components of a CVC Insertion Checklist Operator(s) hand hygiene (alcohol hand rub or antiseptic soap) Chlorhexidine-based skin preparation (allowed to air dry before draping) Maximum sterile barrier precautions for ALL operators (hat, mask, sterile gloves, sterile gown) Full body sterile drape employed Sterility of site/equipment maintained throughout procedure (or procedure stopped and corrective action taken)

CVC Maintenance

• Transparent dressing changed q5–7 d with chlorhexidine skin prep

- Dressing changed immediately if not intact or soiled
- Hubs and needleless access ports disinfected with alcohol or chlorhexidine per standard protocol prior to accessing them

Practices That Do Not Decrease Infection Rate and Should Not Be Routinely Employed	
Antimicrobial ointment at CVC insertion site (except dialysis lines)	
Placement of PICCs rather than central venous catheters (infection rate is the same)	
Systemic antimicrobial prophylaxis	
Routine catheter replacement	
Routine blood cultures drawn through CVC (high false positive rate)	

Adjuncts

- For locations or patient populations with CVC infection rates above target despite adherence to standard prevention measures
- For patients at high risk of severe sequela from a CABSI (limited access, implanted intravascular devices)

Adjunctive Therapies with Proven Benefit	
Daily patient bathing with chlorhexidine	
Use of antimicrobial or antiseptic impregnated catheters	
Chlorhexidine sponge dressings	
Antimicrobial lock therapy	

VENTILATOR-ASSOCIATED PNEUMONIA (VAP)

(Infect Control Hosp Epidemiol. 2008;29:S31)

Definition

• Pulmonary parenchymal invasion by a microorganism in a patient receiving mechanical ventilation for more than 48 hrs

Pathogenesis

Inoculation of the formerly sterile lower respiratory tract by:

- Aspiration of oral secretions
- Colonization of the aerodigestive tract with pathogenic organisms
- Use of contaminated respiratory equipment/medications

Epidemiology

- Rates as high as 10/1,000 ventilator days
- Results in prolonged mechanical ventilation, increased hospital stay, increased cost
- Associated mortality up to 10%

General Principles for VAP Prevention

- Must be institutional priority at leadership level
- Institution wide, standardized education (risk of VAP, consequences of VAP, specific interventions to decrease VAP rate)
- Rigorous adherence to hand hygiene emphasized

- Develop institution wide protocols to prevent contamination of respiratory equipment that follow CDC/AARC guidelines (MMWR. 2004;53:1–36)
- Infection rate monitored and data regularly reviewed by ICU and hospital leadership
- ICU specific compliance rate with selected process measures monitored and regularly reviewed by ICU and hospital leadership

Process Measures To Be Monitored and Reported	
Hand hygiene compliance	
Daily sedation interruption compliance	
Daily assessment of readiness to extubate	
Oral care compliance	
Head of bed elevation compliance	

Specific Interventions Shown to Lower VAP Rates Interventions to Minimize Duration of Mechanical Ventilation

- Utilization of noninvasive ventilation when possible
- Daily assessment of readiness to extubate (formalized protocol)
- Use of weaning protocols
- Daily sedation interruption

Interventions to Minimize Microaspiration and Lower Respiratory Tract Contamination

- Maintain semirecumbent position (head of bed >30 degrees at all times)
- Maintain ETT cuff pressure of at least 20 cm H₂O
- Provide regular oral care with oral antiseptics (chlorhexidine [Peridex] mouthwash) per standardized protocol
- Avoid nasotracheal intubation secondary to risk of sinusitis
- Avoid unplanned extubation and reintubation
- Consider sucralfate rather than acid suppressive therapy for GI bleed prophylaxis (controversial)
- Consider endotracheal tubes with supraglottic suction ports
- Consider use of antiseptic impregnated endotracheal tubes (controversial)
- Consider selective digestive tract decontamination (controversial)

	Practices That Do Not Decrease VAP Rate and Should Not Be Routinely Employed
Prophylact	tic IV antibiotics
Prophylaci	tic aerosolized antibiotics
Intravenou	us immunoglobulin or white-cell-stimulating factors
Rotational	therapy with kinetic beds

VENOUS THROMBOEMBOLISM (VTE) (Chest. 2008;133:381S)

Epidemiology

- DVT rates without prophylaxis range from 10% (medical patients) to 60% (major orthopedic surgery)
- Major cause of morbidity and morality
- Most common cause of preventable in hospital death
- Effective prophylaxis available and most hospitalized patients should receive prophylaxis

• Low rate of clinical bleeding with pharmacologic prophylaxis

Risk Factors for VTE		
Surgery Acute medical illness		
Trauma	Erythropoiesis-stimulating agents	
Cancer	Inflammatory bowel disease	
Venous compression	Nephrotic syndrome	
Immobility	Myeloproliferative disorders	
H/o prior VTE	Obesity	
Pregnancy and post-partum period	Central venous catheterization	
Estrogen containing therapies	Thrombophilia	
Spinal cord injury (SCI)	Hypercoagulable states	

General Principles for an Effective VTE Prevention Program

- Each hospital should develop a formal written VTE prophylaxis policy; patient group specific approach recommended
- Education alone has been ineffective at assuring high compliance rates with VTE policies
- Computer decision support, pre-printed orders, and standard order sets should be used whenever possible
- Periodic audit of compliance and feedback is necessary

Specific Prevention

Pr	ophylactic Options
Agent	Considerations
Mechanical*	Sole agent only in those patients at high risk of bleeding or for neurosurgery patients
Aspirin	Not recommended as sole agent
Low-dose unfractionated heparin (LDUH)	Administer BID to TID
Low-molecular-weight heparin (LMWH)	See product literature for specific dosing
Fondaparinux	Dosage adjustment for renal insufficiency required
Oral Vitamin K antagonist	Target INR: 2-3
Oral direct thrombin inhibitor (dabigatran)	Requires dose adjustment for renal and hepatic insufficiency

^{*}Mechanical devices may be effective when used as adjuncts to pharmacologic measures.

Prophy	laxis by Indication
Minor surgery/mobile medical patients	Aggressive ambulation
Medical patients (bed rest or sick)	LDUH, LMWH, fondaparinux
Most surgical patients undergoing major operations (gen surg, GYN surg, urology)	LDUH, LMWH, fondaparinux
Major orthopedic surgery (hip/knee arthroplasty; hip fracture)	LMWH, fondaparinux, oral vitamin K antagonist, oral direct thrombin inhibitor
Major trauma (including SCI)	LMWH, fondaparinux, oral vitamin K antagonist (unless contra-indicated due to risk of bleeding)
High risk of bleeding	Mechanical prophylaxis (until bleeding risk decreases)

Special Considerations

• Renal impairment

- LMWH, fondaparinux and dabigatran are cleared by kidneys
- Renal function should guide agent choice and dosing regime
- Increased monitoring may be needed for LMWH (anti-factor Xa)
- Neuraxial anesthesia
 - Increased risk of spinal or epidural hematoma must be considered
 - Institution wide guidelines to address common scenarios recommended
- Heparin Induced Thrombocytopenia
 - LMWH has lower rate of HIT than LDUH
 - LMWH cannot be used in a patient with HIT
 - Platelet count monitoring recommended for patients treated with LDUH and LMWH
 - Do not send routine screening HIT test (ELISA) in the absence of clinical suspicion of HIT
- Bariatric surgery
 - Patients may benefit from higher doses of LDUF or LMWH (optimum dosing not well defined)
- Neurosurgery patients
 - Are at increased risk of VTE
 - Intermittent pneumatic compression devices appear effective for VTE prevention in this group
 - LDUH may be used; LMWH may be used but may increase bleeding rate
- Cancer patients
 - 6-fold higher risk of VTE
 - Independent predictor of VTE prophylaxis failure
 - TID LDUH more effective than BID LDUH
 - LWMH also effective; limited cancer specific data for fondaparinux

STRESS ULCERS

Definition

- Mucosal ulceration of esophagus, stomach, or duodenum
- Forms within hours of start of major illness or trauma
- Often multiple superficial lesions; bleeding from capillaries
- Causative factors: impaired mucosal protection from splanchnic hypoperfusion; increased acid secretion in some patients

Epidemiology (Am Health-Syst Pharm. 2005;62:S11)

- Evident on EDG in 75% ICU patients at 72 hrs if prophylaxis is not administered
- Clinically important bleeding (hypotension, orthostasis, hemoglobin drop ≥2 g/dl) in 3%–6% ICU patients
- Overt bleeding in 15% ICU patients without prophylaxis
- Mortality associated with clinically important bleeding is 50%
- Mechanical ventilation >48 hrs and coagulopathy most important risk factors

Risk Factors fo	or Stress Ulcers in ICU Patients	
Mechanical ventilation >48 hrs	Head trauma	
Coagulopathy	Multi-trauma	
Shock	Burns >35% BSA	
Sepsis	H/o GI bleed	
Renal failure	Organ transplantation	
Hepatic failure		

Prophylaxis

- Which Patients:
 - Mechanical ventilation >48 hrs
 - Coagulopathy (platelet < 50 K; INR > 1.5; PTT $> 2 \times \text{normal}$)
 - GI bleeding or ulceration in the last year
 - Two or more other risk factors
- General Principles:
 - Maintain adequate perfusion
 - Pharmacologic prophylaxis for high-risk patients
 - Enteral nutrition when possible (decreases GI bleeding in many studies; not adequate as sole measure)
 - H₂RAs and PPIs may increase the rate of nosocomial pneumonia's (stomach overgrowth with enteric bacteria with microreflux/aspiration)

Pharmacologic	Agents for Stress Ulcer Prophylaxis
Class	Properties
H ₂ receptor antagonists (H ₂ RAs)	PO/IV; increases gastric pH; decreases GI bleeding by >50% vs. placebo
Proton pump inhibitors (PPIs)	PO/IV; increases gastric pH; meta-analysis (CCM. 2010;38:1197) shows minimal, if any, decrease in GI bleeding over H ₂ RA, and no pneumonia difference
Sucralfate	PO only; must get to stomach; improves mucosal barrier function; does not change pH so potentially fewer pneumonias; less effective than H ₂ RAs and PPIs
Antacids	PO; administered q2h; do not work as well as H ₂ RAs or PPIs; electrolyte alterations are common side effects; no longer routinely recommended

- Economic Considerations:
 - H₂RAs and PPIs major budget item for most institutions, many patients receive unnecessarily
 - Treat only those at risk
 - Stop treatment when no longer at risk
 - Use enteral rather than IV formulations whenever possible
 - H₂RAs over PPIs for most patients (more cost effective with little outcome difference)

PRESSURE ULCERS

Epidemiology

- Incidence (acute care setting) 0.4%–38%
- Can cause delayed functional recovery, pain, and infections

- Prolongs hospital stay and associated significant cost of treatment
- Now targeted by CMS and other payment agencies
- Overall paucity of good clinical trials data in field complicates prevention and management strategies for institutions (*JAMA*. 2006;296:974)

Pathogenesis

- Prolonged pressure between a bony prominence and an external surface leads to impaired capillary blood flow and subsequent tissue injury (*JAMA*. 2003;289:223)
- Can develop in 2–6 hrs

Risk Factors for F	Pressure Ulcer Development
External Factors	Patient Specific Factors
Pressure	Immobility
Shear forces (gravitational)	Incontinence
Friction (skin across external surface)	Malnutrition
Moisture	Decreased skin perfusion (hypotension, hypovole- mia, vasopressor use, CHF)
	Microcirculatory impairment (diabetes, peripheral vascular disease, sepsis, etc.)
	Sensory deficit limiting patients ability to detect and respond to tissue injury

Risk Assessment and Mitigation

• Skin assessment and documentation for every patient on admission; daily reassessment

	Pressure Ulcer Staging
Stage I	Intact skin with non-blanchable erythema*
Stage II	Partial thickness skin loss (ulcer, abrasion, shallow crater)
Stage III	Full thickness skin loss (subcutaneous fat may be visible; undermining and tunneling may occur)
Stage IV	Full thickness skin loss with involvement of muscle, fascia, bone, tendon or joint
Unstageable	Base covered with slough or eschar (depth cannot be determined)

^{*}Deep purple or maroon color may indicate deep tissue injury.

- Risk assessment with standardized scoring system such as the Braden or Norton Scale; daily reassessment in the ICU
- Institution of standardized measures for all at risk patients starting at time of hospital admission

Specific Interventions

- Minimize immobility: limit sedation, aggressive early physical therapy, programs to mobilize ventilated patients
- Patient positioning: repositioning at least every 2 hrs (expert opinion) with attention to bony surfaces; must avoid friction and shear forces during repositioning
- Specialized support surfaces

Classifi	ication of Pressure Reducing Sup	port Surfaces*	
Туре	Properties	Best Use	
Static (non-powered)	Mattress or overlay: gel, high- specification foam, air, water	Low-risk patients (least expensive)	
Dynamic (powered) group 1	Alternating pressure mattresses; low air loss mattresses	Moderate- and high-risk patients	
Dynamic (powered) group 2	Air-fluidized mattresses (silicone- coated beads that liquefy with air circulation)	Patients with non-healing stage III and IV ulcers	

^{*}Minimal data available to compare different products; most trials with significant methodologic problems.

- Optimum nutrition full caloric intake with optimum protein balance; no convincing data to support any particular supplement in the absence of known deficiency
- Moisture and incontinence management: goal is to keep skin clean and dry; wicking under-pads, fecal containment systems, barrier creams may be appropriate
- Skin care: dry skin is a risk factor and moisturizers may help; vigorous rubbing and massage can injure skin and should not be used

CATHETER-ASSOCIATED URINARY TRACK INFECTIONS (CAUTI)

Epidemiology

- UTIs are the most common hospital-acquired infection
- 80% attributable to catheter use
- Environmental contamination from bacteriuria may lead to epidemic outbreaks of resistant gram negative infection

Risk Factors for CAUTI	
Duration of catheter use	
Female gender	
Older age	
Failure to maintain a closed drainage system	

General Principles for an Effective CAUTI Prevention Program (Infect Control Hosp Epidemiol. 2008;29:S41)

- Develop processes to decrease catheter insertion rates (define indications, utilize bladder scanners and straight cath techniques for retention)
- Promote timely removal (daily review on rounds; electronic prompts; protocols for nursing directed catheter removal)
- Train personnel for sterile insertion (hand hygiene, sterile gloves and drape, antiseptic cleaning of urethral meatus)
- Train personnel for appropriate maintenance (secure catheter to prevent urethral mucosal injury; hand hygiene prior to system manipulation; maintain sterile closed drainage system; access system aseptically when needed)
- Conduct routine surveillance of CAUTI rates; feedback to local and hospital leadership

Practices not Helpful in Preventing CAUTI; Should Not Be Routinely Employed	
Routine use of silver or antimicrobial impregnated catheters	
Routine urine culture of asymptomatic patients	
Routine treatment of asymptomatic bacteriuria	
Routine systemic antibiotics for prophylaxis	
Routine change of catheter on a set schedule	
Continuous bladder irrigation with an antimicrobial (as a preventive measure)	

NOSOCOMIAL TRANSMISSION OF METHICILLIN-RESISTANT STAPHYLOCOCCUS AUREUS (MRSA) (Infect Control Hosp Epidemiol. 2008;29:S62)

Epidemiology

- >60% of hospital associated S. aureus infections are methicillin-resistant
- MRSA infection associated with higher mortality, longer length of stay and higher cost of care compared to MSSA infection
- Asymptomatic MRSA colonization common
- Colonized patients: 29% risk of developing active MRSA infection within 18 mo

Hand Hygiene

- Colonized or infected patients contaminate their environment
- MRSA can spread from person to person via healthcare workers' hands
- Universal compliance with hand hygiene fundamental to prevention of spread of MRSA and other nosocomial pathogens
- Hand hygiene compliance should be monitored and reported

Identification of MRSA Colonized or Infected Patients

- Hospitals need automated systems to promptly identify affected patients
- Contact precautions instituted for these patients: private room (cohort if not available), gown and gloves to enter room with gown and gloves removed to exit room; strict enforcement of hand hygiene
- Work processes and environment must be modified to promote compliance
- Active surveillance (nasal swabs) for units or patient populations with high endemic MRSA rates and for control of active outbreaks
- Some data supports decolonization therapy in certain patient populations

Environmental Control

- Patients with MRSA contaminate their environment and care equipment; leads to transmission of MRSA to other patients
- Institutional protocols for daily/terminal cleaning can reduce transmission
- Attention to high-touch areas important (bed rails, carts, commodes, doorknobs)
- Dedicate patient equipment when possible (stethoscopes, etc.)
- Routine chlorhexidine bathing of ICU patients associated with decreased MRSA infections and decreased MRSA transmission (reduction in environmental contamination)

DAILY ASSESSMENT: FAST HUGGS (CCM. 2005;33:1225; NEJM. 1995;332:1338)

- Feeding: can the patient be fed orally, if not enterally? If not, should we start parenteral feeding?
- Analgesia: the patient should not suffer pain, but excessive analgesia should be avoided
- Sedation: the patient should not experience discomfort, but excessive sedation should be avoided; "calm, comfortable, collaborative" is typically the best level. Try to avoid benzodiazepines use
- Thromboembolic prevention: should we give low-molecular-weight heparin or use mechanical adjuncts?
- Head of the bed elevated: optimally, 30–45 degrees, unless contraindications (e.g., threatened cerebral perfusion pressure)
- Ulcer prophylaxis: usually H₂ antagonists; sometimes proton pump inhibitors (consider the risk of increased of clostridium difficile infection) (*Arch Int Med.* 2010;170:772)
- Glucose control: maintain a blood glucose target of 180 mg/dl or less and avoid hypoglycemic episodes (*NEJM*. 2009;360:1283)
- Geriatric: delirium evaluation, ADL evaluation, early mobilization, early occupational and physical therapy, review of medications, removal of restraints (e.g., CVC physical restraints, chemical restraints, urinary catheters)
- Social: involvement of social worker, identification of surrogate decision maker or proxy, clarification of DNR/DNI orders

ADVANCED CARDIAC LIFE SUPPORT (ACLS)

SAMUEL M. GALVAGNO, JR., DO, PhD • DRAGOS M. GALUSCA, MD

For the management of trauma patients see Chapters 15 and 16.

UPDATED 2010 AHA GUIDELINES (Circulation. 2010;122:S729–S767)

Figure 1. ACLS Cardiac Arrest Algorithm

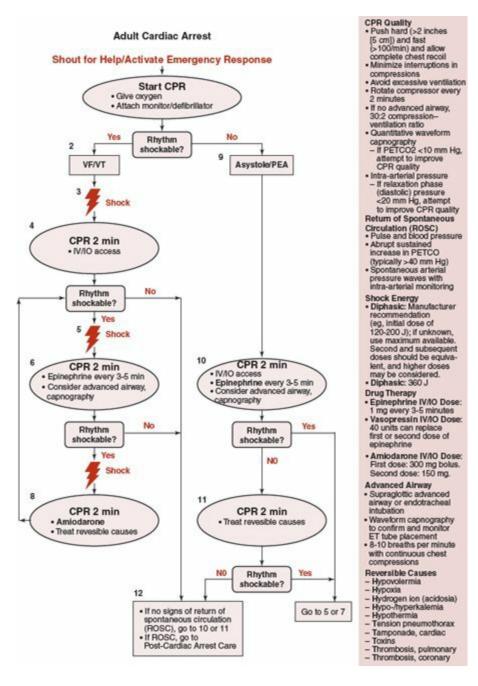


Figure 2. ACLS Cardiac Arrest Circular Algorithm

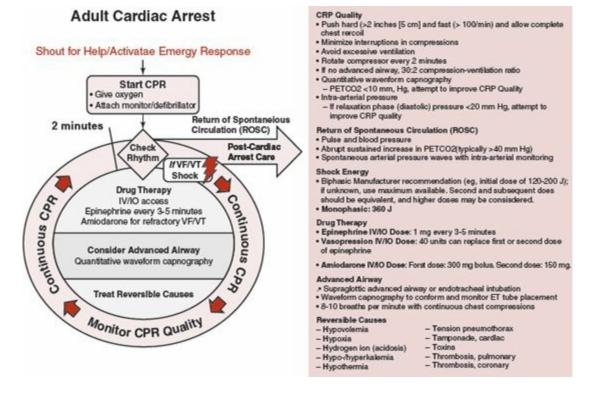


Figure 3. Bradycardia Algorithm

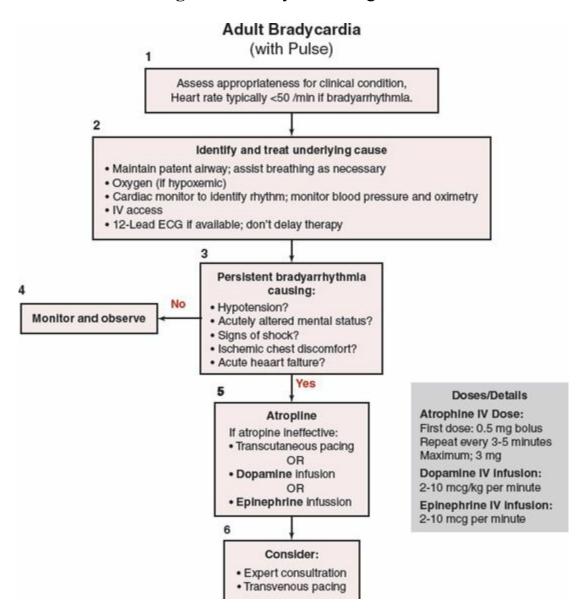
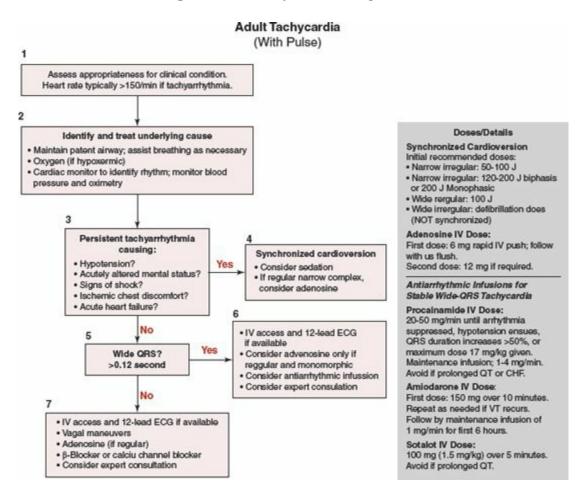


Figure 4. Tachycardia Algorithm



GENERAL TRAUMA I

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Trauma Organization and ATLS Guidelines

- Over 60 million injuries occur in the United States each year.
- Trimodal death distribution: Immediate, early and late deaths.
- For every trauma death 3 patients suffer permanent disability.

	Time Frame	Typical Injury
Immediate deaths	Seconds to minutes after injury	Apnea due to severe brain injury, high spinal cord injury, rupture of heart or great vessels
Early deaths	Minutes to several hours after injury	Subdural or epidural hematoma, hemopneu- mothorax, intra- abdominal organ injury, pelvic fracture
Late deaths	Several days to weeks after injury	Sepsis and multiple organ system dysfunc- tion

Principles of Advanced Trauma Life Support (ATLS)

- Treat the greatest threat to life first
- The lack of a definitive diagnosis should never impede the application of an indicated treatment
- A detailed history is not essential to begin the evaluation of an acutely injured patient

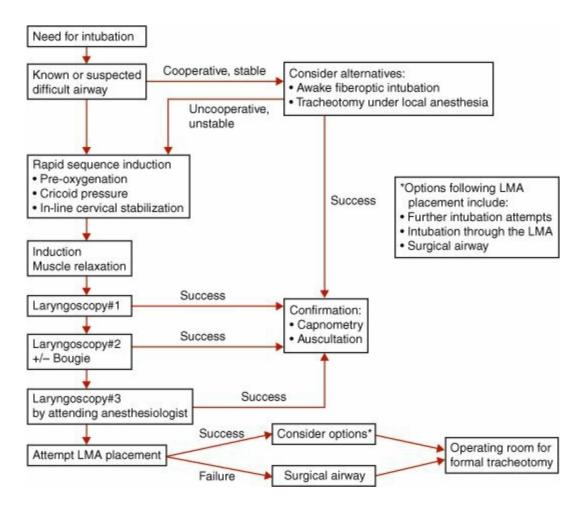
Initial Assessment and Management

- Preparation → triage → primary survey (ABCDEs) → resuscitation → adjunct to primary survey and resuscitation → secondary survey (head-to-toe evaluation and history) → adjuncts to secondary survey → continued postresuscitation monitoring and reevaluation → definitive care
- Primary Survey: lifesaving measures are initiated when the problem is identified

	Components of	Primary Survey (ABCDEs)
A	Airway maintenance with cervical spine protection	Patency, GCS < 9 requires definitive airway, assume C-spine injury
В	B reathing and ventilation	Observe bilateral rise and fall and auscultate
С	Circulation with hemor- rhage control	Assess blood volume and cardiac output (level of consciousness, skin color, pulse) and control external hemorrhage
D	Disability: neurologic status	GCS, pupillary size and reaction, lateralizing signs and spinal cord injury level
E	Exposure/Environmental control	Completely undress patient, but prevent hypothermia

Figure 1. Emergency Airway Management Algorithm Used at the R. Adams Cowley Shock Trauma

Center



From Stephens CT, Kahntroff S, Dutton RP. The success of emergency endotracheal intubation in trauma patients: A 10-yr experience at a major adult trauma referral center. *Anesth Analg.* 2009;109:866–872.

GENERAL APPROACH

Primary Survey

- The sequence for the primary survey is remembered with the acronym "ABCDE"
- A: (Airway) rapid assessment of the airway, including inspection for foreign bodies and facial, mandibular, or tracheal/laryngeal fractures
 - The most common cause of airway obstruction is altered level of consciousness, allowing the tongue to block the posterior pharynx
 - Emergency endotracheal intubation is indicated for:
 - Airway obstruction, hypoventilation, severe hypoxemia (despite supplemental oxygen), GCS < 8, cardiac arrest, severe hemorrhagic shock
 - Emergency airway management algorithm
 - Rapid sequence intubation is the standard of care for securing the airway in trauma patients
 - The need for a surgical airway has been reported to be as low as 0.3% (*Anesth Analg.* 2009;109:866)
 - Key points in modified algorithm for maxillofacial and neck trauma: stopping is seldom an option, a surgical airway may be the best choice in certain situations, an awake intubation can be used in a patient with a known difficult airway if the patient is cooperative and stable (*Anesthesiology Clin*. 2007;25:1)
- B: (Breathing) contingent upon the integrity of the phrenic nerve and brainstem, the bony chest, and

chest contents

- Exam findings suggestive of a thoracic injury: penetrating wound, shortness of breath, respiratory distress, chest wall crepitance/tenderness, tracheal deviation, jugular venous distension
- If unstable hemodynamically, place chest tube on injured side
 - Do not wait for chest X-ray
 - Consider cefazolin 2 g IV prior to insertion
- C: (Circulation) palpation of pulses provides immediate information regarding circulatory status
 - Systolic blood pressure estimations:
 - Radial pulse: 90 mm Hg
 - Brachial pulse: 80 mm Hg
 - Femoral pulse: 70 mm Hg
 - Carotid pulse: 60 mm Hg
 - Heart rates >120/min can represent approximately 30% blood loss; rates >140 can represent >40% blood loss
 - Emergency-release blood products should be administered for hemodynamically unstable patients who have failed to respond to 2 l of crystalloid infusion or have ongoing blood loss
 - If type-specific blood is unavailable, give type O packed cells
 - To avoid sensitization in women of childbearing age, give type O, Rh-negative cells
 - Type-specific blood is usually available within 10 min
 - Type-specific blood is compatible with ABO and Rh blood types (not tested for other antibodies)
 - Hypovolemic shock should NOT be treated with vasopressors, steroids, sodium bicarbonate, or continued crystalloid infusion. It should be treated with blood products and operative control.
 - For further transfusion guidelines see section G: Life Threatening Hemorrhage, Hemorrhagic Shock.
- D: (Disability) assess gross motor movement in all extremities and calculate a Glasgow Coma Score (GCS)
 - GCS: Eye (4 points), Verbal (5 points), Motor (6 points)
 - Eye: (4) eyes open spontaneously (3) eye opening to verbal command (2) eye opening to pain (1) no eye opening
 - Verbal: (5) oriented (4) confused (3) inappropriate words (2) incomprehensible words (1) no verbal response
 - Motor: (6) obeys commands (5) localizes pain (4) withdrawals from pain (3) flexion to pain decorticate response (2) extension to pain decerebrate response (1) no motor response
- E: (Exposure) removal all of the patient's clothes, including underwear
 - Stabilize the cervical spine
 - Perform rectal exam to evaluate for gross blood or a high-riding prostate
 - Immediately cover and warm patient to prevent heat loss
 - Adjuncts to primary survey: cardiac monitoring, urinary and gastric catheter, AP chest and pelvis X-ray

Secondary Survey

- Secondary survey: begins when primary survey is complete, resuscitative efforts well established and the patient demonstrates normalization of vital signs
 - Head-to-toe evaluation

- Each region of the body completely examined
- Reassessment of all vital signs
- Complete neurologic examination is performed
- History (AMPLE) A Allergies, M Medications, P Past illness/Pregnancy, L Last meal, E
 Events/Environment related to injury
- Adjuncts to the secondary survey: specialized diagnostic tests, X-rays, CT scans, Urography, angiography, ultrasound, bronchoscopy, esophagoscopy as indicated
- Reevaluation: after any intervention and frequently to assure new findings are not overlooked.
- Definitive care: the closest appropriate local facility should be chosen based on its overall capabilities (See B. Triage and Surveillance)

CERVICAL SPINE CLEARANCE

- CT scan is indicated for the following:
 - Age >65, fall >3 ft or 5 stairs, motor vehicle crash at high speed, motor vehicle rollover or ejection, bicycle crash, motorcycle crash, motorized recreational vehicle crash
- If no injury or fracture seen on cervical spine CT, cervical collar must remain on if a patient has any of the following:
 - Altered mental status, intoxication with drugs or alcohol, traumatic brain injury, midline cervical tenderness, focal neurological deficit, numbness or paresthesia of any extremity without direct injury, painful distracting injury
 - An MRI should be considered in these instances if the patient remains obtunded to rule out ligamentous injury
 - If no ligamentous injury is identified with MRI, and the CT for the cervical spine is negative, the collar may be removed in obtunded patients
- If a patient is cooperative and doesn't meet any of the abovementioned conditions, a clinical exam may be performed
 - The cervical collar may be removed in the absence of:
 - No midline cervical pain or limitation with active flexion or extension
 - No midline cervical pain or limitation with active rotation to the left or right
 - If there is pain with active range of motion, a spine surgery consult should be obtained, flexion/extension radiographs may be considered
 - If the radiographs are negative for evidence of subluxation or fracture, the collar may be removed
- If a fracture or ligamentous injury is identified at any point with the abovementioned studies and clinical exams, a spine surgeon should be consulted

FOCUSED ASSESSMENT WITH SONOGRAPHY FOR TRAUMA (FAST)

- Four-view abbreviated ultrasound technique
 - View 1: right upper quadrant hepatorenal fossa (Morrison's pouch)
 - View 2: sub-xyphoid view to detect pericardial fluid
 - If unable to obtain, may position probe in left second intercostal space, midclavicular line

- View 3: left upper quadrant to detect peri-splenic fluid
- View 4: pelvis retrouterine pouch (pouch of Douglas) and retrovesical pouch
- Interpreted as positive, negative, or indeterminate
- Exam is directed at identifying the presence of free intraperitoneal or pericardial fluid, usually due to hemorrhage
- Sensitivity varies between 42–96%
 - Specificity is often higher
- Potential benefits of FAST (Postgrad Med J. 2010;86:285):
 - May reduce the number of diagnostic peritoneal lavages (DPL)
 - Marginal reduction in need to obtain CT
 - Reduces time to initial diagnosis and time from emergency department to operating room
- Potential pitfalls of FAST:
 - Is a "rule-in" triage tool for patients with blunt abdominal trauma
 - CT remains the gold standard for blunt abdominal trauma
 - May be non-effective or misleading in untrained hands
 - Some have recommended 200 scans to obtain proficiency (*J Trauma*. 1999;46:466)
 - Images are not as complete and reproducible as CT
 - Free fluid in the pelvis can be missed without a full bladder
 - Important organ injuries that will require surgery can be missed
 - Misses retroperitoneal hemorrhage
 - Misses peri-nephric and peri-aortic hemorrhage
 - Limited in obese patients or with subcutaneous emphysema

NUTRITIONAL SUPPORT FOR TRAUMA PATIENTS

- Early nutrition helps maintain host defenses and preserves lean body mass in trauma patients (*J Trauma*. 2004;57(3):660)
 - There is no proven benefit of starting enteral feedings within 24 hrs of admission versus within 72 hrs of admission
 - In patients undergoing laparotomy for abdominal injuries, direct small bowel access should be obtained
 - A nasojejunal or gastrojejunal feeding tube, or feeding jejunostomy should be placed
- Patients with blunt and penetrating abdominal injuries should be fed enterally when possible
 - Beneficial effects include prevention of sepsis, preservation of gut mucosa and prevention of bacterial translocation, prevention of pneumonia, and prevention of abscess formation
- Total parenteral nutrition (TPN) should be considered by post-injury day 7 if enteral feeding is not feasible
- Patients who cannot tolerate 50% of their goal enteral nutrition rate should be started on TPN by post-injury day 7 until >50% of the goal rate for enteral nutrition is achieved
- Enteral nutrition is not advised in patients who are incompletely resuscitated
 - Intestinal necrosis and aspiration are possible
- Early gastric feeding is feasible for trauma patients and outcomes are equivalent for patients fed into the duodenum
 - Patients at high risk for aspiration should receive feedings into the jejunum

VENOUS THROMBOEMBOLISM (VTE) PROPHYLAXIS IN TRAUMA

- Risk factors for VTE in trauma patients are:
 - Spinal cord injuries
 - Lower extremity fractures
 - Severe head injuries
 - Injury Severity Score (ISS) >8
 - Shock at the time of admission (systolic blood pressure <90 mm Hg)
 - Any surgical procedure lasting more than 30 minutes
 - Femoral venous line insertion
 - Prior deep vein thrombosis (DVT) or pulmonary embolism (PE)
- In patients with risk factors, pharmacological prophylaxis is recommended (*J Trauma*. 2002;53(1):142)
 - Low-dose unfractionated heparin (5,000 Units subcutaneously three times daily) is one recommended approach
 - The optimal dose of heparin has not been established
 - DVT risk may be decreased by up to 25% with this approach
 - The risk for pulmonary embolism may be reduced by over 50%
 - There is little evidence to support a benefit of low-dose heparin as the *sole* agent for VTE prophylaxis in trauma patients
 - The use of low molecular weight heparin (LMWH) has been shown to be more efficacious than low-dose unfractionated heparin
 - Some studies in the general surgery literature show a clear benefit of LMWH over unfractionated heparin
 - LMWH is recommended for trauma patients with:
 - Pelvic fractures requiring operative fixation or prolonged bed rest (>5 days)
 - Complex lower extremity fractures requiring operative intervention and prolonged (>5 days) bed rest
 - Spinal cord injury with complete or incomplete motor paralysis
 - These patients must not have other injuries that predispose them for a high risk of bleeding
- Serial ultrasound (duplex) exams in high risk asymptomatic trauma patients should be considered to screen for DVTs
- If a patient is freely ambulatory, and has no risk factors, VTE pharmacological VTE prophylaxis is not required; TEDs and SCDs should be used
- Contraindications to pharmacological prophylaxis:
- High risk of bleeding
- Pelvic or retroperitoneal hematoma
 - Ocular injury with hemorrhage
 - Some traumatic brain injuries (acute phase)
 - Solid organ injury
 - Systemic anticoagulation
 - INR \geq 1.5, or aPTT ratio \geq 1.3
 - Platelet count <50,000
 - Allergy; history of heparin-induced thrombocytopenia

For patients with these contraindications, TEDs/SCDs should be used until the contraindication no longer exists

- Serial duplex surveillance scans should be ordered
- Consider vena cava filter placement in high-risk trauma patients
- Contraindications for enoxaparin are: renal failure, renal insufficiency (creatinine clearance <30 ml/min), indwelling epidural catheter

VENA CAVA FILTERS FOR VTE PROPHYLAXIS IN TRAUMA PATIENTS

- Vena caval filters (IVC filters) have been shown to be efficacious for preventing PE in trauma patients
- Indications include:
 - Recurrent PE despite full anticoagulation
 - Proximal DVT and contraindications to full anticoagulation
 - Proximal DVT and major bleeding while on full anticoagulation
 - Progression of iliofemoral clot despite anticoagulation (rare)
- "Extended" indications for prophylactic vena cava filter placement in a patient with established DVT or PE include:
 - Large free-floating thrombus in the iliac vein or IVC
 - Following massive PE in which recurrent emboli may prove fatal
 - During/after surgical embolectomy.
- Insertion of a "prophylactic" IVC filter should only be considered in very high risk trauma patients who cannot receive anticoagulation because of increased bleeding risk, and have one or more of the following injury patterns:
 - Severe closed head injury (GCS < 8)
 - Incomplete spinal cord injury with para or quadriplegia
 - Complex pelvic fractures with associated long-bone fractures
 - Multiple long-bone fractures

TRAINING IN TRAUMA

- Intensive care providers should complete the American College of Surgeons' Advanced Trauma Life Support (ATLS) course (http://www.facs.org/trauma/atls).
- Evidence-based practice guidelines for the management of traumatically injured patients are maintained and updated by The Eastern Association for the Surgery of Trauma (EAST; http://www.east.org).

SCORING SYSTEMS IN TRAUMA

Please see Chapter 18 for the use of the Glasgow Coma Scale (GCS), and Chapter 12 for the details of the scoring systems used to asses injury severity for trauma patients.

Triage and Surveillance

- Triage: process of rapidly and accurately evaluating patients to determine the extent of injuries and the appropriate level of medical care required
- Civilian triage: the patient with the most life threatening, but survivable, injuries given priority, as resources permit
- Military triage: patient who can survive with the smallest amount of resources given priority
- Mass casualty triage: victims separated into critical, urgent, delayed or expectant (dead or expected to die)
- Undertriage: transporting to a facility that does not have appropriate resources for a given patient.
 - May result in increased mortality or morbidity from delays in definitive care
 - 5% undertriage rate considered acceptable (American College of Surgeons Committee on Trauma guidelines)
- Overtriage: transporting to a higher level of care than necessary based on injuries
 - little impact to patient but strain on resources
 - in order to reduce risk of undertriage, overtriage rate of 50% acceptable (American College of Surgeons Committee on Trauma guidelines)
- Trauma Center Classification

	Classification and Capabilities of Trauma Centers
Level I	Capable of providing total care for every aspect of injury. Maintains resources and personnel for patient care, education and research
Level II	Provides comprehensive trauma care regardless of injury severity. May supplement the activity of a Level I trauma center
Level III	Offers prompt evaluation, resuscitation, emergency surgery and stabilization and when needed transportation to higher level of care
Level IV	Rural facility that supplements care provided within the larger trauma system. Must have 24 hr emergency coverage

Criteria for transfer to trauma center (Morb Mortal Wkly Rep. 2009;58(RR-1):1)

- Physiologic Criteria
 - Glasgow Coma Scale <14
 - Systolic blood pressure <90 mm Hg
 - Respiratory rate <10 or >29 breaths/min or <20 in an infant <1 yr
- Anatomic Criteria
 - Penetrating injury of the head, neck, torso and extremities proximal to the knee or elbow
 - Flail Chest
 - 2 or more long bone fractures
 - Crushed, degloved or mangled extremity
 - Amputation proximal to the wrist and ankle
 - Pelvic fractures
 - Open or depressed skull fractures
 - Paralysis
- Mechanism of Injury Criteria
 - Fall >20 ft for adult, or >10 ft or 2–3 times child's height for child <15 yrs
 - High risk MVC
 - Intrusion > 12 in. into occupants side, or > 18 in. to any site
 - Partial or complete ejection from motor vehicle

- Death in same passenger compartment
- Vehicle telemetry data consistent with high risk for injury
- Auto vs. pedestrian/bicyclist thrown, run over, or with impact at >20 mph
- Motorcycle crash >20 mph
- Special considerations: consider transfer to a trauma center if
 - Age >55 or <15
 - Anticoagulation or bleeding disorder
 - Burns
 - Time sensitive extremity injury
 - End-stage renal disease requiring dialysis
 - Pregnancy of more than 20 wks
 - EMS provider judgment

Immediate Life Threatening Trauma Conditions

Tension Pneumothorax

- One way valve forms, air forced into thoracic cavity without means of escape
- Clinical diagnosis, do not delay treatment for X-ray confirmation
 - Needle thoracentesis: large caliber needle into the second intercostal space, midclavicular line of the affected hemithorax

Massive hemothorax

• Rapid accumulation of more than 1,500 ml of blood in the chest cavity

Cardiac tamponade

- Pericardium fills with blood from heart, great vessels, or pericardial vessels, restricting cardiac activity
 - Pericardiocentesis: large gauge catheter 1–2 cm inferior and to the left of the xiphochondrial junction at 45 degree angle to skin, advance needle cephalad while aspirating and aim toward the tip of the left scapula. Aspirate as much fluid as possible. If extreme ST-T wave changes or widened QRS complex pull back needle until normal EKG reading returns. Leave catheter in place, place 3-way stopcock

Pelvic Fracture

• Disruption of the posterior osseous—ligamentous complex, tearing of the pelvic venous plexus, and disruption of the internal iliac arterial system

Immediate	ly Life Threatening Trauma	a Conditions	
Problem	Assessment	Management	
Tension pneumothorax	Tracheal deviation Distended neck veins Absent breath sounds Tympany on percussion	Needle decompression Tube thoracostomy	
Massive hemothorax	Tracheal deviation Flat neck veins Absent breath sounds Dullness on percussion	Venous access Volume replacement Surgical consultation Tube thoracostomy	
Cardiac tamponade	Distended neck veins Muffled heart sounds Ultrasound findings	Pericardiocentesis Venous access Volume replacement Pericardiotomy Thoracotomy	
Pelvic fracture (open book or vertical shear)	Unstable pelvis	Volume replacement Decrease pelvic volume wrap pelvis in sheet Orthopedic consultation Angiography External fixation	

Principles of Damage Control Surgery

- Definition: the rapid surgical control of hemorrhage and contamination, temporary closure, resuscitation to normal physiology in the ICU, and subsequent re-exploration and definitive repair
- Goal: to restore normal physiology rather than normal anatomy
- When to employ damage control surgery
 - Multiple life threatening injuries
 - Acidosis, pH < 7.3
 - Hypothermia, temperature <35°C
 - Coagulopathy nonmechanical bleeding
 - Massive transfusion
 - Hypotension and shock on presentation
 - Combined hollow viscous and vascular injuries
 - Mass casualty
- Primary operation and hemorrhage control: control hemorrhage and contamination; explore to determine extent of injury, therapeutic packing, and temporary abdominal closure.

Critical Ca	re Considerations in Damage Control Surgery	
Core rewarming	Warm patient, room, ventilation gases and all fluids	
Reversal of acidosis	Aggressive resuscitation with crystalloid, colloid and blood product Generally avoid sodium bicarbonate unless pH < 7.2	
Reversal of coagulopathy	Aggressive replacement with blood products 1:1:1 ratio of PRBC to FFP to platelets in massive hemorrhage See section F. Life Threatening Hemorrhage, Hemorrhagic Shock	
Avoidance of abdominal com- partment syndrome (ACS)	Monitor intra-abdominal pressure See section E. Abdominal Compartment Syndrome	

- Planned reoperation: typically 24–48 hrs after injury. Must coincide with reversal of hypotension, acidosis, hypothermia and coagulopathy
 - Unplanned reoperation: ongoing bleeding, missed enteric injury resulting in systemic

- inflammatory response syndrome and shock, ACS
- This may take place in the operating room, or at the ICU bedside if patient not stable enough for travel

Rhabdomyolysis

	Compartment Syndrome
Definition	Tissue pressure exceeds perfusion pressure in a closed anatomic space
Causes	Fracture, crush injury, penetrating injury, hemorrhage, burn, any high energy trauma, prolonged lying on a limb
Locations	Hand, forearm, upper arm, abdomen, buttocks, upper leg, lower leg, foot
Signs/ symptoms	Pain out of proportion to exam, pain with passive stretching of muscle (early sign), paresthesia, pale and/or cool skin, pulselessness (very late finding), tense compartment
Consequence	Tissue damage, muscle necrosis, nerve injury, functional impairment, renal failure, death
Treatment	Surgical fasciotomy of all associated compartments. Permanent damage by 6 hrs

- Anterior compartment of the lower leg-deep peroneal nerve sensation in web space between first 2 toes
- Compartment pressures measurement: not required for diagnosis. Generally >30 mm Hg warrants intervention

	Rhabdomyolysis
Definition	Breakdown of skeletal muscle fibers resulting in release of myoglo- bin into bloodstream
Causes	Trauma, crush injury, electrical shock, burn injury, CPR, ischemia/reperfusion, hypothermia, medications and illicit drugs, compartment syndrome
Signs/ symptoms	Myalgias/pigmenturia ↑ Serum CK, myoglobin, potassium, urea, phosphorus arrhythmia
Consequence	Free myoglobin toxic to renal tubules \rightarrow acute renal failure Hyperkalemia \rightarrow arrhythmia
Course	CK levels peak 2–5 d post-injury Levels >16,000 U/L more likely to cause renal failure Hypocalcemia from influx/deposition of calcium in damaged muscles
Therapy	Restore perfusion IV fluids: maintain urine output ~200 cc/hr until CK ↓ No evidence for mannitol/sodium bicarbonate/lasix Treat hypocalcemia if tetany/severe hyperkalemia develops Treat compartment syndrome if it develops Dialysis if fluid resuscitation fails to correct intractable hyperkalemia and/or acidosi

(This table is from Johnson D. Trauma, Burn, and Critical Care Managment. Pocket Anesthesia)

Abdominal Compartment Syndrome

- An increase in the volume of any abdominal or retroperitoneal contents causes an increase in intraabdominal pressure (IAP)
- IAP in normal hospitalized patients ranges from 0–13 mm Hg (*ANZ Journal of Surgery*. 2006; 76:1106)
- Markedly increased IAP leads to intra-abdominal hypertension (IAH)

- The clinical condition that results from the organ dysfunction that occurs with IAH is termed ACS
- IAH = intra-abdominal pressure >12 mm Hg
- ACS = intra-abdominal pressure >20 mm Hg with evidence of end-organ dysfunction

Types of Abdominal Compartment Syndromes			
Primary ACS	Secondary ACS	Recurrent ACS	
Injury or disease that originates inside the abdomen	Due to conditions outside the abdomen – sepsis, capil- lary leak, burns, massive fluid resuscitation	Development of ACS after suc- cessful surgical treatment of primary or secondary ACS	

(Malbrain ML, Cheatham ML, Kirkpatrick A, et al. Results from the International Conference of Experts on the Intra-abdominal Hypertension and Abdominal Compartment Syndrome. I. Definitions. Intensive Care Medicine. 2006;32:1722–1732. PMID: 16967294)

13	Abdominal Compartment Syndrome
Definition	Intra-abdominal pressure >20 mm Hg with evidence of end-organ dysfunction
Causes	Abdominal trauma, ruptured AAA, hemorrhagic pancreatitis, burns, sepsis
Signs/symptoms	Tense distended abdomen, elevated intra-abdominal pressure, decreased cardiac output, inadequate ventilation with elevat- ed peak airway pressures, hypoxia and hypercarbia and renal dysfunction
Definitive treatment	Decompressive laparotomy

Bladder pressure – most common indirect measure of intra-abdominal pressure.

50 cc of saline is instilled into the urinary bladder through the Foley catheter. The tubing of the collecting bag is then clamped, and a needle is inserted into the specimen-collecting port of the tubing proximal to the clamp and is attached to a manometer. The transducer is zeroed at the level of the symphysis pubis.

• Bladder pressure inaccurate in setting of intraperitoneal adhesions, pelvic hematoma or fracture, neurogenic bladder (*Ann Surg.* 1984;199:28)

System	Cause	Consequence
Cardiovascular	Compression of heart via dia- phragm – ↓ compliance, ↓ con- tractility, ↑ SVR, Compression of IVC – ↓ venous return	Cardiac output CVP, PCWP (not reflective of volume status)
Pulmonary	Compression of lungs via diaphragm, inflammatory cytokines	↓ FRC ↑ PIP ↑ Shunt fraction, dead space Hypoxia, hypercarbia, atelectasis and edema
Renal	Compression of renal vein Arterial vasoconstriction from sympathetic nervous and renin – angiotensin systems	Oliguria to anuria
Gastrointestinal	Compression of portal and mesenteric veins	Intestinal edema Lactic acidosis Bacterial translocation
Central Nervous System	Possible impaired venous drainage from cerebral outflow	Intracranial pressure Cerebral perfusion pressure

Treatment of ACS

- The only definitive treatment is immediate decompressive laparotomy
- Early surgical consult

Initial Management		
Evacuate intraluminal contents	Nasogastric decompression Rectal tube decompression Stop or reduce enteral nutrition	
Evacuate intra-abdominal space occupying lesions	Surgical evacuation of clot In certain situations consider catheter drainage	
Improve abdominal wall compliance	Ensure adequate sedations/analgesia Consider paralytic Remove constrictive dressings/eschar Position reverse Trendelenburg	
Optimize fluid administration	Avoid excess fluid resuscitation Aim for 0 to negative fluid balance by day 3 Fluid removal by judicious diuresis if stable Consider hemodialysis, ultrafiltration	
Optimize systemic/regional perfusion	Goal-directed fluid therapy Hemodynamic monitoring to guide resuscitation Consider pressors to maintain perfusion pressure	

Life Threatening Hemorrhage, Hemorrhagic Shock

- Hemodynamically unstable trauma patients are bleeding until proven otherwise
- Trauma patients should receive NO MORE than 2 L crystalloid (ATLS)
- Common traumatic causes of hemorrhagic shock: solid abdominal organ injury, myocardial or major vessel laceration, pelvic and femoral fractures and scalp lacerations
- Lethal triad: hypothermia, coagulopathy, acidosis
- Do not delay surgical control of hemorrhage

Clas	sification of Sho	ck Based on a 7	0 kg Adult Ma	ale
	Class I	Class II	Class III	Class IV
Blood loss (ml)	<750	750-1500	1500-2000	>2000
Blood loss (% blood volume)	<15%	15–30%	30–40%	>40%
Heart rate	<100	100-120	120-140	>140
Blood pressure	Normal	Normal	Decreased	Decreased
Pulse pressure	Normal/ Decreased	Decreased	Decreased	Decreased
Respiratory rate	14-20	20-30	30-40	>40
Urine output (ml/kg)	>30	20–30	5–15	<5
Mental status	Slightly anxious	Mildly anxious	Confused	Lethargic/ Obtunded
Fluid replace- ment	Crystalloid	Crystalloid	Crystalloid and blood	Crystalloid and blood

From the ATLS for Doctors textbook. American College of Surgeons Committee on Trauma. ATLS Student Course Manual. 8th edition. Chicago, IL: American College of Surgeons, 2008, 61.

From the ATLS for Doctors textbook. American College of Surgeons Committee on Trauma. ATLS Student Course Manual. 8th edition. Chicago, IL: American College of Surgeons, 2008, 61.

Transfusion

• 1:1:1 ratio of PRBC to FFP to platelets is associated with improved survival compared to previous

- transfusion strategies (J Trauma. 2007;63:805).
- Use uncrossmatched blood products in unstable patient if necessary.
- Type-specific blood products when immediately available
- Revert to standard restrictive transfusion practice after bleeding is controlled

Agents that decrease coagulopathic bleeding

- Recombinant factor VIIa reduced blood product use in refractory traumatic hemorrhage but did not affect mortality compared with placebo (*J Trauma*. 2010;69:489)
- No established effective factor VIIa dose in trauma (17–400 mcg/kg reported)
- Complications of hemorrhage/massive transfusion
- Hypothermia
 - Leads to ↓ citrate metabolism, ↓ hepatic metabolism, ↓ drug clearance, ↓ synthesis of acute phase proteins, ↓ production of clotting factors
 - 10% decrease in coagulation factor activity for each 1°C drop in temperature
 - Warm the patient, fluids, room
- Coagulopathy
 - Dilutional and consumptive coagulopathy and thrombocytopenia
 - 1:1:1 transfusion ratio PRBC to FFP to platelets
 - Recombinant factor VIIa: binds to exposed tissue factor, \(\tau\) conversion of factor X to Xa. Can reduce PRBC requirement in bleeding trauma patients unclear if improved survival
- Electrolyte abnormalities
 - Hypokalemia, hyperkalemia: KCl concentration in PRBC from 7–77 meq/L
 - Hypocalcemia, hypomagnesemia: each unit of PRBC contains 3 g citrate which binds Ca⁺⁺ and Mg⁺⁺, must measure ionized Ca⁺⁺ (not total serum)
 - Monitor closely and correct as needed
- Acidosis/alkalosis: average pH in PRBC 7.0. Citrate metabolized to bicarbonate leads to metabolic alkalosis after massive transfusion
 - Metabolic acidosis therefore indicates tissue hypoperfusion, not the result of transfusion
 - Sodium bicarbonate for severe metabolic acidosis with hemodynamic instability or renal failure
- Transfusion reaction: cumulative risk of all transfused products
- Transfusion-associated acute lung injury (TRALI)
 - Occurs 1 in 5,000 units PRBC, 1 in 2,000 units FFP and 1 in 400 units platelets (*Transfusion*. 2003;43(8):1053)
 - Supportive care

GENERAL TRAUMA II

PETER J. FAGENHOLZ, MD • GEORGE KASOTAKIS, MD • GEORGE VELMAHOS, MD, PhD

AIRWAY TRAUMA

Initial management focuses on airway control, testing to define extent of airway injury, and identification of associated injuries.

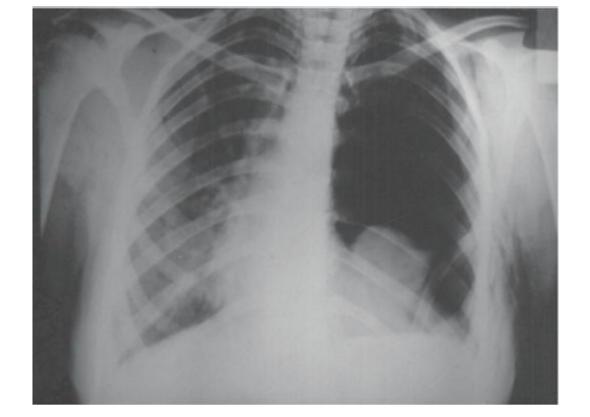
Investigations for Airway Trauma Clinical Examination

- Unstable face and malocclusion are signs of facial fractures which may compromise the supraglottic airway
- Stridor, impaired phonation (including "breathy" voice), cervical tenderness or ecchymosis suggest cervical laryngotracheal injury
- Subcutaneous emphysema and hemoptysis
- Pneumomediastinum or pneumothorax with their associated physical findings can occur with intrathoracic airway injury

Chest X-ray

- Can often be obtained before any other diagnostic test
- Look for pneumothorax and subcutaneous or mediastinal air
- If pneumothorax persists after chest tube placement with ongoing air leak, this suggests major bronchial injury. Lungs collapse away from the hilum towards the diaphragm suggesting complete mainstem bronchial transection
- Disruption of the tracheal air column or overdistension of the endotracheal tube balloon may be seen with tracheal disruption

Figure 1. "Fallen Lung" Collapsing Away from the Hilum Towards the Diaphragm After Left Main Bronchus Disruption



Fiberoptic Laryngoscopy and Bronchoscopy

- Mainstay of laryngeal evaluation in the awake patient protecting their airway
- Endotracheal tube (small, 6.5–7.5 for adults) should be loaded over bronchoscope in case findings mandate immediate intubation
- Most sensitive method to evaluate for distal airway injury

Computed Tomography (CT)

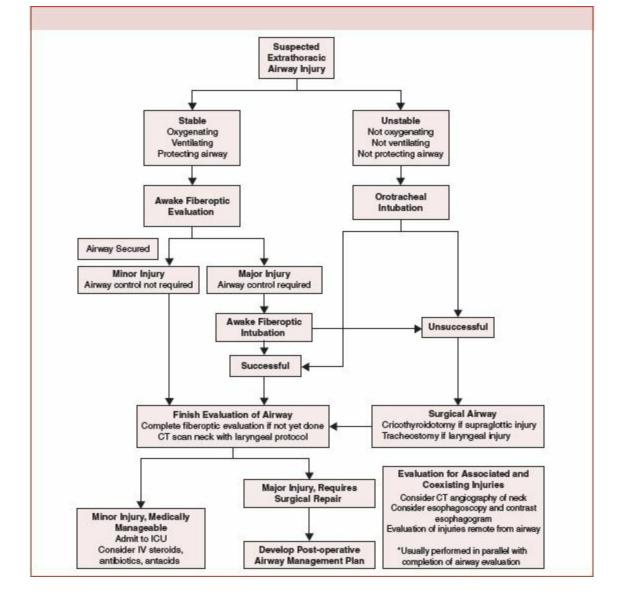
- Should not be undertaken until airway is secured, either by tracheal intubation, or when examination and prior tests indicate that patient can protect their own airway

 Neels CT is vital to identify presence of and alignment of large goal fractures. CT can also identify
- Neck CT is vital to identify presence of and alignment of laryngeal fractures. CT can also identify associated cervical injuries (e.g., cervical vascular or spinal injury)
- Facial and chest CT can help define associated injuries, but are less important than bronchoscopy for evaluating the airway itself

Initial Management of Airway Trauma

Sections 1 and 2 are summarized by this algorithm in Figure 2.

Figure 2. Algorithm for Management of Suspected Extrathoracic Airway Injury



Supraglottic Injury

- Injury to the midface, mandible, or soft tissues of the oropharynx or nasopharynx can compromise the patient's ability to maintain an adequate airway
- When anatomy is distorted by injury and the patient is maintaining her own airway, rapid sequence intubation can turn a stable situation into an unstable situation. If intubation is required, use awake fiberoptic technique or proceed directly to a surgical airway
- If patient is in extremis and not protecting her airway → attempt orotracheal intubation. If orotracheal intubation fails → place a surgical airway
- If patient is oxygenating, ventilating, and protecting her airway → perform awake fiberoptic examination and intubation if necessary. If awake fiberoptic intubation fails and intubation is required, proceed directly to surgical airway

Cervical Laryngotracheal Injury

- In suspected laryngotracheal trauma, if the patient is oxygenating, ventilating, and protecting their airway → perform fiberoptic laryngoscopy/bronchoscopy. If significant injury is identified, intubate over bronchoscope. If there is only minor or no injury, do not intubate and obtain a CT scan
- In suspected laryngotracheal trauma, if the patient is not oxygenating and ventilating → attempt orotracheal intubation while simultaneously preparing for surgical airway. If orotracheal intubation

is successful, perform bronchoscopy to evaluate distal airway. If unsuccessful, or resistance is met, abort → perform surgical airway

- Avoid supralaryngeal devices such as laryngeal mask airway or esophageal obturator airway, as they may distort anatomy, worsen subcutaneous edema, or convert partial airway disruption to complete disruption
- In penetrating injuries if the open end of the disrupted trachea is visible in the wound, it can be directly intubated

Intrathoracic Airway Injury

- Most distal airway injuries are from blunt trauma, often near the origin of the mainstem bronchus
- Distal injuries often present with pneumothorax. If pneumothorax after blunt trauma is treated with tube thoracostomy and a large air leak is present, airway injury must be considered
- Early detection is important to avoid late stricture formation
- Bronchoscopy is the best method to evaluate for distal airway injury

Definitive Therapy for Airway Trauma Supraglottic Pharyngeal Injury

- Repair of facial/pharyngeal injuries should precede removal of any artificial airway
- Steroids often used if edema contributes significantly to airway compromise
- Tracheostomy can provide a definitive airway

Cervical Laryngotracheal Injury

- All cervical airway trauma should be admitted to ICU, with the possible exception of an isolated, non-displaced hyoid bone fracture in an otherwise stable patient
- Grade I and most grade II laryngeal injuries can be managed non-operatively. Surgical repair is standard for grades III–V

Grading of Laryngeal Injury		
Grade I	Minor endolaryngeal hematoma; minimal airway compromise, if any; no detectable fractures	
Grade II	Endolaryngeal hematoma or edema associated with compromised air- way; minor mucosal lacerations without exposed cartilage; non-displaced fracture shown on CT scan	
Grade III	Massive endolaryngeal edema with airway obstruction; mucosal tears with exposed cartilage; immobile vocal cord(s)	
Grade IV	Same as III with more than 2 fracture lines on imaging studies; massive derangement of endolarynx	
Grade V	Laryngotracheal separation	

- All patients should have head of bed elevation, voice rest, humidified air, antacids (H₂ blockers or PPIs), and initially be kept NPO
- If mucosal tears or cartilaginous fractures of the larynx are identified, antibiotics are recommended, usually broad spectrum for at least 5 days
- Steroid use is controversial, they are often used to decrease swelling after laryngeal injury
- If surgical repair is indicated (grade III–V injury), it should be performed immediately
- Tracheostomy is commonly performed after laryngeal repair
- Immediate post-operative extubation is preferred after cervical tracheal repair

Intrathoracic Airway Injury

• Intrathoracic injury is repaired by thoracotomy

- In cases of iatrogenic trauma to the membranous posterior tracheal wall (from endotracheal intubation with bougie or during percutaneous tracheostomy) small injuries may be manageable non-operatively
- Immediate post-operative extubation is preferred whenever feasible after airway repair

THORACIC TRAUMA

Investigations in Thoracic Trauma Clinical Examination

- External signs of trauma including chest wall ecchymosis, bony deformity, paradoxical respiratory motion, and subcutaneous emphysema
- Neck examination should focus on tracheal position, and presence of subcutaneous air or jugular venous distension
- Note location of entry and exit wounds in penetrating trauma
- Absent or decreased breath sounds suggest pneumo- or hemothorax

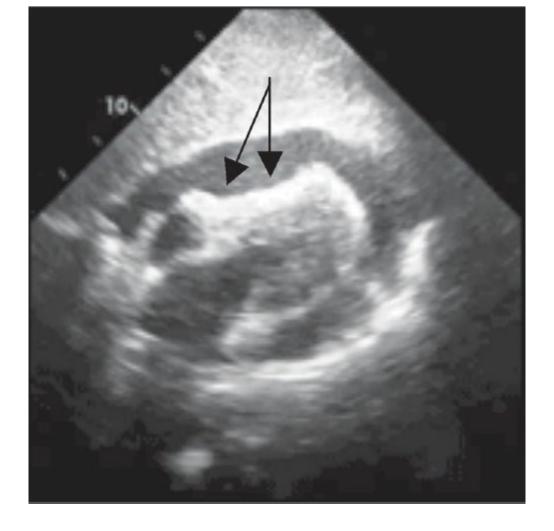
Chest X-ray

- Rapidly available
- Identifies large hemothorax, pneumothorax, or pneumomediastinum. Can suggest aortic injury if mediastinum is widened
- Can assess position of central venous catheters or tubes (ETT, CVC, chest tubes)

Ultrasound

- Allows early identification of pericardial tamponade (see figure)
- Can also identify hemothorax and pneumothorax as part of extended focused abdominal sonography for trauma (E-FAST)

Figure 3. Ultrasound Image of Pericardial Effusion Causing Tamponade. Arrowheads are in the Pericardial Effusion



Chest CT

- Most sensitive test for hemothorax, pneumothorax
- Can identify intrathoracic vascular injuries
- Can assess chest wall injury and pulmonary contusion
- Identifies associated spine injuries

Other

- Angiography may better define vascular injury if CT is equivocal
- Barium swallow and esophagoscopy can further evaluate suspected esophageal injury
- Subxiphoid pericardial window has essentially been replaced by ultrasound. Can diagnose tamponade if ultrasound equivocal or unavailable. Should generally only be performed if definitive thoracotomy immediately available

Specific Injuries Cardiac Trauma

- Blunt
 - Must be suspected in all patients with blunt precordial trauma
 - Spectrum of injury is wide including cardiac rupture, pericardial rupture with cardiac herniation, valve injury, papillary or chordae tendineae rupture, septal injury, and blunt coronary injury. By far the most common is myocardial contusion
 - EKG is useful for screening a completely normal EKG in a hemodynamically stable patient eliminates the need for any further testing

• In hemodynamically unstable patients, or patients with an abnormal EKG, a FAST followed, if there is no tamponade, by an echocardiogram should be obtained. Any injuries requiring repair (e.g., tamponade, valvular) can then be addressed. A pulmonary artery catheter may guide management if cardiogenic shock persists without an addressable anatomic lesion

• Penetrating

- Should be actively investigated in all patients with penetrating precordial or transmediastinal wounds. FAST/echocardiogram is the first test of choice
- Usually present with tamponade
- Thoracotomy required for repair. Repair is performed without cardiopulmonary bypass
- Post-operative echocardiogram should be performed to evaluate for valvular lesions, septal defect, or other endocardial injuries

Great Vessel Injury

- Includes injury to the aorta and its brachiocephalic branches, pulmonary vessels, superior or intrathoracic inferior vena cava, and innominate and azygos veins
- Penetrating injuries typically present with massive hemorrhage, which must be immediately surgically addressed
- In stable patients CT angiography is the single most useful diagnostic modality
- Blunt injuries are often contained, and are increasingly amenable to endovascular stenting

Chest Wall and Lung Injury

- Chest wall
 - Chest X-ray and CT are the diagnostic cornerstones
 - Age, number of rib fractures, and bilaterality are risk factors for respiratory failure after chest wall injury
 - Analgesia is critical to avoiding respiratory failure in patients with chest wall injury. If moderate pain does not respond to enteral or parenteral NSAIDs and narcotics, or severe pain is present at presentation, proceed to regional blocks. Epidural or paravertebral blocks are appropriate depending on patient status (coagulopathy, hemodynamics) and local expertise
 - Surgical fixation of rib fractures in selected patients may improve short-term (pneumonia, time spent on ventilator) and long-term (chronic pain) outcomes
- Pneumothorax
 - Pneumothorax results from injury to the lung (e.g., laceration by projectile or fractured rib, tear from deceleration) or entrainment of air from the outside, as in a sucking chest wound
 - Small pneumothoraces can be observed, even in patients on positive pressure ventilation. Large pneumothoraces or those causing respiratory or cardiovascular compromise are treated with tube thoracostomy. The chest tube can be removed after the air leak resolves
- Hemothorax
 - Hemothorax can originate from intrathoracic great vessels, lacerated chest wall blood vessels, or lung parenchyma
 - Initial treatment is with tube thoracostomy. If chest tube drains >1,500 ml blood initially or >200 ml/hr \times 4 hrs, bleeding is unlikely to stop without thoracotomy
 - Retained hemothorax after trauma can be treated with thrombolytics instilled via a chest tube or with thoracoscopy and evacuation. If a large retained hemothorax is not drained it can result in empyema, recurrent effusions, or fibrothorax with impaired pulmonary function

Esophageal Injury

• Esophageal injury is rare. Over 80% of esophageal injuries are from penetrating neck trauma and

involve the cervical esophagus

- Signs and symptoms are nonspecific (hoarseness, hematemesis, subcutaneous air, dysphagia) and delayed treatment is associated with poor outcome, so index of suspicion must be high
- Esophagoscopy and a contrast esophagogram together are highly sensitive for ruling out esophageal injury—neither modality alone is adequate. Neck and chest CT can show secondary signs such as pleural effusion, pneumomediastinum, or abscess
- Injuries are usually repaired primarily. Broad spectrum antibiotics, gastric decompression, and antacids are standard. In severe injuries, distal enteral access (such as tube jejunostomy) should be considered early

ABDOMINAL TRAUMA

Investigations for Abdominal Trauma

Clinical Examination

- Still the most important diagnostic tool in the awake, cooperative patient. Intubation, use of sedatives and pain killers may hamper a reliable examination
- Rigidity, involuntary guarding and rebound tenderness (worsening pain upon release of pressure) are clinical signs of peritonitis
- Seat-belt marks are associated with >20% of intra-abdominal injuries
- Pain referred to the left (Kehr's sign) or right shoulder is suggestive of splenic or hepatic injury, respectively, from irritation of the diaphragm

Chest X-ray

- A plain, semi-upright (with the patient in reverse Trendelenburg), chest X-ray is part of abdominal evaluation because thoracic trauma is commonly associated
- Look for subdiaphragmatic air (hollow viscus injury), lower rib fractures (consider associated splenic, hepatic, renal injuries), an elevated diaphragm or hollow viscus in the chest (diaphragmatic rupture)

Focused Abdominal Sonography for Trauma (FAST)

- Ultrasound of the pericardium, bilateral paracolic gutters and pelvis
- May reveal free fluid in these areas (potentially the source of bleeding in the hemodynamically unstable polytrauma victim)
- Disadvantages: no visualization of the retroperitoneum, operator dependent. Has largely replaced DPA and DPL (Diagnostic peritoneal aspiration and lavage) as the optimal method for ruling out intraperitoneal bleeding

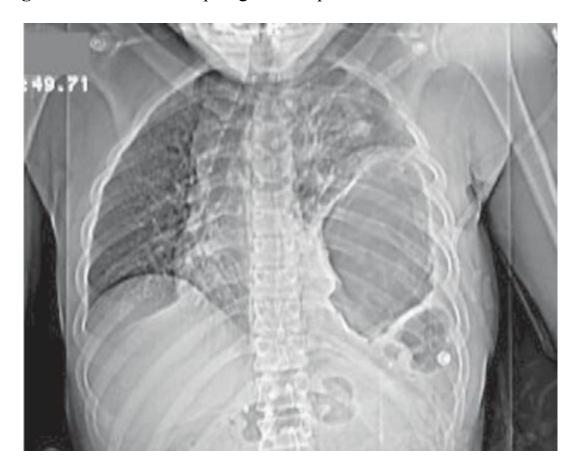
Abdominal and Pelvic CT

- Among the most reliable studies to evaluate abdominal trauma
- Assesses fascial penetration in stab wounds, delineates the bullet trajectory in gunshot wounds, demonstrates free air or fluid in the peritoneal cavity
- Rather insensitive in diagnosing hollow viscus injuries (free fluid in the absence of solid organ trauma, free air, bowel wall thickening, mesenteric stranding) and diaphragmatic trauma
- Addition of IV contrast with appropriate timing of scanning helps identify arterial or venous injuries; delayed contrasted images can identify urinary tract injuries (delayed contrast extravasation from the kidneys or the bladder)

Specific Abdominal Injuries Diaphragmatic Injuries

- Diaphragmatic rupture can occasionally be seen on plain chest X-rays with herniation of abdominal contents to the chest; more commonly subtle injury that can be detected by maintaining a high index of suspicion
- Fine cut CT or selective use of diagnostic laparoscopy aid diagnosis
- The left side is far more commonly involved than the right (Figure 4)

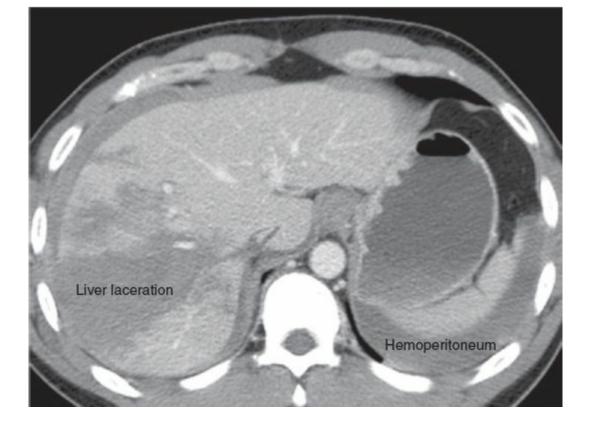
Figure 4. Traumatic Diaphragmatic Rupture with Intrathoracic Stomach



Liver Injuries

- Most commonly injured abdominal organ in both blunt and penetrating trauma (Figure 5)
- Follow patients with serial hemoglobin levels. Almost all liver injuries not needing emergent exploration because of hemodynamic instability can be successfully managed non-operatively
- Angiographic embolization is a useful adjunct of non-operative management
- Complications, such as bilomas or biliary ascites, hemobilia (connection between an artery and the biliary tree), and intrahepatic collections occur mostly in high-grade injuries and can also be managed non-operatively

Figure 5. Liver Laceration with Associated Hemoperitoneum on CT



Splenic Injuries

- Commonly associated with left lower rib fractures
- In contrast to the liver, non-operative management of splenic trauma fails in up to 15%. High-grade injuries fail more frequently
- Rebleeding may occur late and can be catastrophic
- Angioembolization has a role in the absence of associated intra-abdominal injuries in the hemodynamically stable patient with persistent transfusion requirements
- Vaccination against *Streptococcus pneumonia*, *Haemophilus influenza*, *Neisseria meningitidis* is recommended in patients with splenectomy or splenic artery embolization, however the timing remains controversial

Pancreatic Injuries

- Typically seen in association with upper lumbar spine fractures and duodenal (proximal) or splenic (distal) injuries
- Diagnosis: CT scan and elevated pancreatic enzymes (low sensitivity and specificity). A repeat CT scan 12–24 hrs later enhances diagnostic accuracy
- Low-grade injuries can be managed non-operatively
- Assessment of integrity of the main pancreatic duct is essential: in the absence of ductal trauma, drainage is usually adequate; ductal injuries distal to the superior mesenteric vessels are managed with distal pancreatectomy, while head and proximal body injuries are treated with damage control principles in unstable patients (suturing, draining, packing) or with a pancreateduodenectomy in stable patients

Hollow Viscus Injuries

- The small bowel is the most commonly injured hollow viscus
- High association with other intra-abdominal injuries
- Small and large bowel injuries are typically repaired primarily. If >50% of the bowel circumference is involved, local resection and primary anastomosis can be performed. Proximal

diversion if significant hemodynamic instability

• Antibiotics (ideally a 2nd generation cephalosporin with anaerobic coverage, i.e., cefotetan) do not need to be continued beyond 24 hrs perioperatively

Urologic Injuries

- Macroscopic and persistent microscopic hematuria requires evaluation of the urinary tract typically with CT scanning, including delayed contrasted images
- Renal injuries are managed non-operatively in the hemodynamically stable patient, while ureteral injuries are most commonly repaired primarily over stents
- Bladder injuries are managed depending on their location: intraperitoneal injuries require operative repair, whereas extraperitoneal injuries are managed with prolonged catheterization and drainage
- In the presence of blood at the meatus, a high riding prostate or perineal/scrotal hematoma, a retrograde urethrogram should be obtained. If injury is confirmed, long-term catheterization is indicated

Pelvic Fractures

- Can lead to life-threatening bleeding from disruption of the extensive retroperitoneal venous plexus or less commonly from arterial trauma
- Initial management requires decreasing the volume of the pelvis with a pelvic binder or external fixator
- Angiographic embolization is effective in controlling arterial bleeding. Preperitoneal pelvic packing is an alternative technique reserved for hemodynamically unstable patients or settings without angiographic capabilities

Vascular 1njuries

- Inferior vena cava injuries can be repaired or ligated, if below the renal veins
- Temporary control of arterial injuries can be achieved by shunts
- PTFE grafts or autologous venous grafts are appropriate for arteries that cannot be repaired primarily
- Blunt injuries (if not bleeding) can be managed with percutaneous stents

Abdominal Compartment Syndrome (see Chapter 15)

EXTREMITY INJURIES

- Always obtain plain X-rays to rule out bony injuries
- Bone fractures require stabilization through splinting and operative fixation
- Open fractures present an emergency and mandate irrigation, debridement and antibiotic coverage
- Associated neurovascular injuries have to be screened for: as soon as the clinical situation permits, a careful neurologic examination should be performed to assess for subtle signs of neurologic injury; any suspicion of vascular injury should be screened with measurement of the ankle—brachial (ABI) or brachial—brachial index (BBI). ABI < 0.9 or BBI < 1 should prompt CT angiography of the affected extremity
- Soft tissue crush injuries are also a consideration: crushed muscle releases nephrotoxic substances and can cause compartment syndrome (see below). Management includes trending of serum CPK and urine myoglobin levels and adequate hydration (maintain urine output >0.5 ml/kg/hr). In severe cases (CPK > 15,000) consider urine alkalinization with a NaHCO₃ drip

Extremity Compartment Syndrome

- Due to increased pressure in the extremity muscular compartments, >20–25 mm Hg
- More common in the lower extremities
- Results from crush injuries, extremity vascular trauma followed by ischemia and reperfusion injury, or due to massive resuscitation
- Pain out of proportion to injury and paresthesias. Swollen extremity, and the compartments are tense. Loss of pulses and sensorimotor function (late findings). Maintain higher index of suspicion in sedated, intubated patient
- Pressures are assessed with a Stryker needle monitoring device
- Treatment consists of fasciotomies of all compartments of the affected extremity

Fat Embolism Syndrome (FES)

- Release of fat globules from the bone marrow. May lead to multiple organ failure from a direct embolic effect or from the release of inflammatory mediators
- Most commonly associated with long bone fractures. Related to the fracture itself or reaming and manipulation during repair
- Respiratory failure (from a worsening ventilation—perfusion mismatch), altered mental status and/or seizures (from fat emboli-induced cerebrovascular accidents) upper body petechial rash and subconjunctival or retinal hemorrhages
- Diagnosis is difficult and typically made on clinical grounds. Sudan stain may identify fat particles in the urine and BAL washings may demonstrate >5% of cells staining positive for fat. However, neither of the two tests are sensitive or specific
- Treatment is supportive

BURN MANAGEMENT

EMILY Z. KEUNG, MD • JOAQUIM M. HAVENS, MD

Advances in initial resuscitation, critical care and surgical management of burns have led to dramatic improvements in the overall survival and quality of life of the burn patient. Initial evaluation of the burn patient follows the same systematic assessment of all trauma patients with additional attention to critical areas of airway management, fluid management and wound care.

Anatomy and General Principles

The skin is composed of two distinct layers.

- Epidermis: outer layer, acts as barrier, provides thermal regulation, protects against infection, UV light, and evaporation of fluids
- Dermis: inner layer, provides durability and elasticity
- Epidermis and dermis separated by basement membrane zone: BMZ plays significant role in burn wound healing, anchoring structures, protect epithelialized wounds from shear injury
- Epidermis will recover if viable dermis present → one goal of burn wound care is to maintain dermal viability

A burn is tissue injury resulting from exposure to thermal, electrical, chemical, or radioactive agents

- Zones of injury
 - Zone of coagulation: central, most severely damaged, cells here are coagulated or necrotic
 - Zone of stasis: area characterized by vasoconstriction and ischemia, cells initially viable but may convert to coagulation as a consequence of development of edema, infection, decreased perfusion
 - Zone of hyperemia: characterized by vasodilatation resulting from release of inflammatory mediators, typically viable

Evaluation of the Burn Patient

Always begins with initial systematic primary and secondary survey to evaluate for any traumatic injuries, as in Chapter 15.

- Type of injury, heat source, circumstances of injury.
 - Thermal: most common type of burn, from contact with extreme heat
 - Electrical injuries: may present with little injury to skin but significant injuries to muscle, vasculature, and bone; cardiac standstill or arrhythmia complications; myonecrosis common, monitor for signs and symptoms of rhabdomyolysis (see Chapter 15)
 - Chemical:
 - Acids → coagulation necrosis, hydrofluoric acid burns cause calcium/magnesium chelation, risk of cardiac arrest
 - Alkali → liquefaction necrosis, vascular thrombosis, dermal ischemia
 - Scalds: burn from hot water or steam, may be seen in child/elder abuse

Clean burn wound with soap and water, remove debris.

Assess extent of wounds and total body surface area (TBSA) involved: "Rule of nines".

- Estimates surface area in adult patients
- Head and each upper extremity represent 9% TBSA each
- Anterior trunk, posterior trunk and each lower extremity represent 18% TBSA each
- Less accurate in children due to different body proportions

Assess depth of burns

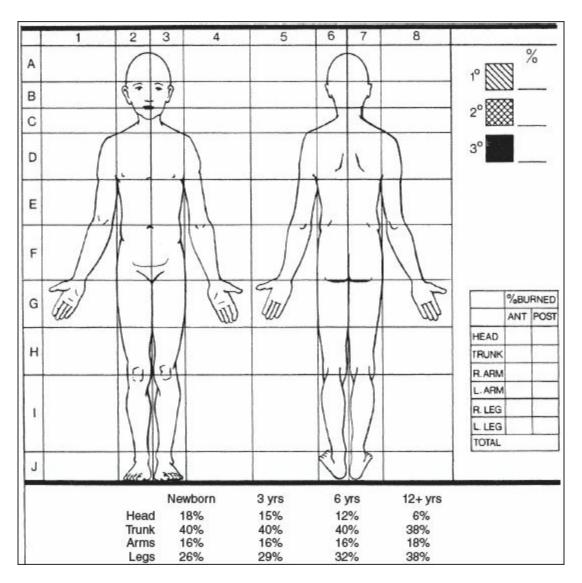
Airway and Respiratory Management in Burns

Deliver maximal FiO₂ during initial resuscitation.

Inhalation injuries: inhalation of hot gases may cause direct injury to airway without obvious signs to head/neck, associated with increase in mortality and morbidity.

- Risk of inhalation injury increased if voice change, carbonaceous sputum, singed nasal hairs, swelling of nose/mouth/lips/throat, history of being in enclosed space
- Low threshold for intubation: perform before progression of airway edema prevents safe intubation, should be considered for patients presenting with stridor
- Carboxyhemoglobin level taken within 1 hr after injury indicative of smoke inhalation if >10%

Figure 1. Example of One of a Number of Age-Specific Burn Diagrams Available to Facilitate Accurate Estimation of the Extent of a Burn, Compensating for Anthropometric Differences Between Age Groups



Ove	rview of Burn Wound Mana	gement
Depth of Burn	Clinical Features	Management
Superficial/first degree	Dry, erythematous, blanches with pressure, painful	Soothing, moisturizing lotions
Partial thickness/second degree	Blisters, pink, moist, blanches with pressure, painful	Greasy gauze
Deep partial thickness/ second degree	Blisters, wet or waxy, patchy color, less painful	Silver sulfadiazine, surgical excision and grafting if not going to heal within 3 wks
Full thickness/third degree	Dry, leathery, black or white, does not blanch, painless	Silver sulfadiazine, early excision and skin grafting
Fourth degree	Extends into fascia and/or muscle	

Fluid Management in Burns (Crit Care Med. 2009;37:2819)

- Cardiac output is reduced immediately post burn (decreased circulating volume and myocardial depression). 3–5 d post burn → hypermetabolic state (increased cardiac output, decreased SVR).
- Resuscitation goal is to anticipate and prevent burn shock. Delay in fluid resuscitation increases mortality however excessive resuscitation and volume overload also deleterious → can lead to pulmonary edema, conversion of superficial burns to deeper burns, compartment syndrome (extremities, abdominal) and need for fasciotomies.
- Factors that influence fluid requirement during resuscitation include: age, TBSA, burn depth, inhalation injury, associated injuries, delay in resuscitation, fasciotomies.
- Lactate Ringer's solution most closely resembles normal body fluids.
- Resuscitation should be titrated to hemodynamics and urine output (goal 0.5 ml/kg/hr in adults, 0.5–1.0 ml/kg/hr in children <30 kg), often will need more than estimated by Parkland formula.
 - Parkland formula: 4 ml of lactated Ringer \times kg \times % TBSA burn in the first 24 hrs
 - Give half of calculated fluid given in first 8 hrs post burn, remainder over the next 16 hrs (example: 70 kg man with 50% TBSA burns needs $4 \times 70 \times 50 = 14,000$ ml; give 7,000 ml during 0–8 hrs after burn, then 7,000 ml over the next 8–24 hrs after burn)
- No clinical advantage with colloids or hypertonic saline; some studies show increased mortality and complications with these.

Dressings and Topical Antimicrobial Agents Used in Burn Care

- Burn dressings include silver-containing dressings, biologics, and skin substitutes.
- Dressings containing nanocrystalline silver embedded provide some broad-spectrum antibacterial activity: Acticoat (polyethylene mesh), Aquacel AG (hydrofibers), Mepilex AG (soft silicone dressing)
- Biologic dressings for temporary wound coverage: allograft, xenograft
- Skin substitutes: integra (outer layer of Silastic film protective barrier which is removed after dermal inner layer has become incorporated into wound over time)

	Topical Ag	ents Used in Burn Ca	are
Agent	Antimicrobial Coverage	Advantages	Disadvantages
Bacitracin, Xeroform	Gram positive	Soothes, moisturizes, good for facial care and epithelializing wounds	Not appropriate for deeper wounds
Mafenide	Broad-spectrum antibacterial, anticlostridial	Penetrates eschar well	Painful on application, carbonic anhydrase inhibition → metabolic acidosis
Mupirocin	Anti-MRSA	MRSA coverage	Narrow antimicrobial coverage
Silver nitrate	Broad-spectrum antibacterial	Effective for prophylaxis and treatment of wound infection	Poor eschar penetration, hyponatremia, methemo- globinemia
Silver sulfadia- zine	Broad-spectrum antibacterial, antipseudomonal	Soothes on application, not painful	Poor eschar penetration, leucopenia

(Sterling JP, Heimbach DM, Gibran NS. Management of the Burn Wound. In: Souba WW, ed. ACS Surgery: Principles and Practice. 6th ed. New york, NY: WebMD Professional Publishing, 2007:1425.)

Surgical Burn Wound Management

Early excision and skin grafting: decrease risk of burn wound sepsis, attenuates systemic inflammatory response syndrome.

- Full-thickness skin grafts: less contraction but will leave greater dermal deficit at donor site increasing length of time needed for healing and increased risk of hypertrophic scarring
- Split-thickness skin grafts: these will contract

Escharotomy: may be required for circumferential full-thickness extremity burn wounds in which distal perfusion is compromised or chest burns in which eschar poses external mechanical barrier to respiration.

Metabolism and Nutrition

- Hypermetabolic response to burns can result in life-threatening protein-calorie malnutrition. Increase in normal resting energy expenditure is compounded by insensible losses through wound bed and protein loss/leaking into interstitial space.
- Enteral nutrition (nasogastric, gastric or intestinal tube) is preferred as this maintains intestinal integrity, associated immunity and limits complications of TPN.
- Indirect calorimetry considered "gold standard," however results affected by oxygen therapy, hemodynamic instability, fever.
- Many formulas exist for estimating basal energy expenditure \rightarrow adjust by stress factor of 1.2–2.
- Harris Benedict equation: estimates basal energy rate.
 - Male: $kcal/d = 66.5 + (13.8 \times weight in kg) + (5 \times height in cm) (6.76 \times age in yrs)$
 - Female: $kcal/d = 655 + (9.6 \times weight in kg) + (1.85 \times height in cm) (4.68 \times age in yrs)$

	Macronutrients
Protein	1.5-2.0 g protein/kg/d
Carbohydrate	5-7 mg/kg/min of glucose representing 50% of total cal/d
Fat	Fewer than 15% of non-protein calories from fat

- Vitamin A, C, D in standard multivitamin formulations, trace minerals (selenium, zinc, copper.)
- Glutamine (0.35 gm/kg/d) may ↓ infectious complications, ↓ hospital length of stay, ↓ mortality
- Anti-catabolic/anabolic agents:
 - Oxandrolone: promotes protein synthesis, nitrogen retention (*Burns*. 2003;29:793)
 - Beta blockade/propranolol: decrease heart rate, reduce cardiac index (*N Engl J Med.* 2001; 25:1223)

Complications

- Burn wound sepsis: risk decreased by early excision, confirm diagnosis by biopsy.
- Abdominal compartment syndrome: suggested by urinary bladder pressure >20 mm Hg, can contribute to respiratory and renal failure and bowel ischemia, may require celiotomy and leaving abdominal compartment open (See Chapter 15)
- Extremity compartment syndrome: may require escharotomy, fasciotomy (See chapter "Trauma").
- Pneumonia: avoid prophylactic antibiotics as they increase risk of wound infections with resistant organisms.
- DVT: increased risk for DVT, prophylaxis as with trauma patients unfractionated heparin or low-molecular-weight heparin, but pay attention to renal function.
- Stress ulcer: prophylactic H₂ receptor blocker or proton pump inhibitor.
- Hypothermia: dramatic loss of the thermal regulation properties of skin, can contribute to coagulopathy and hemodynamic instability, institute warming measure, warm room, forced air heating, fluid warmer.

HEAD TRAUMA AND SPINAL CORD INJURY

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TRAUMATIC BRAIN INJURY (TBI)

Traumatic brain injury (TBI) requires early diagnosis, management of primary injury, and prevention of secondary injury. Morbidity and mortality from secondary injury may exceed that of primary injury.

Neurologic Assessment

• Determine level of consciousness with Glasgow Coma Scale (GCS) score for stratification of injury severity, management strategies, and need for intervention (*Lancet*. 1974;2:81)

		Glas	gow Coma Scale		
	Motor		Verbal	E	ye Response
6	Spontaneous, obeys command				
5	Localizes pain	5	Coherent, oriented		
4	Withdraws to pain	4	Confused	4	Spontaneous
3	Flexion to pain	3	Inappropriate	3	Opens to voice
2	Extension to pain	2	Incomprehensible	2	Opens to pain
1	None	1	None	1	None

	7	Fraumatic Head Injury Classification	on
Injury Severity	GCS	Criteria	Management
Minimal	15	Neurologically intact No loss of consciousness No amnesia	No CT head required No hospitalization required
Mild	14	Brief loss of consciousness <5 min Mild memory impairment	CT head (abnormal in 16%)
Moderate	9–13	Loss of consciousness >5 min Neurologic deficit	CT head, ± surgical intervention
Severe	3–8	Severe neurologic deficit	CT head, ± surgical intervention

- Focal injury results from restricted vector of force delivered to an intracranial region; includes: epidural hematomas, subdural hematomas, cerebral contusions, intraparenchymal hematomas, and subarachnoid hemorrhage
- Diffuse injury results from wide force vectors and high acceleration/deceleration injuries; includes: concussion, diffuse axonal injury (DAI), post-traumatic coma
- Surgical intervention is guided by a combination of radiographic findings as well as clinical exam, such that patients with significant neurologic deficits or with minor neurologic alteration but

expanding hematomas both merit surgery

Prognosis

- Severe TBI has ~30% mortality; 16% of the survivors have severe neurological deficits; 3% remain in a persistent vegetative state. Risk factors for poor outcome include older age, low GCS, poor pupil response or anisocoria, poor motor response, hypoxia, hypotension, coagulopathy, and significant CT characteristics (*J Neurotrauma*. 2007;24:329).
- Intensive neurorehabilitation improves functional outcomes, with 85% of recovery occurring within the first 6 mo after injury (*Lancet Neurol.* 2008;7:728).

Initial Management

- Prehospital considerations: shorter transfer time to the hospital as well as management at Level 1 regional trauma centers improves outcome in TBI (*Prehospital Emergency Care.* 2007; S12)
- ABCs: secure airway, ensure adequate oxygenation, avoid hypotension
- Provide adequate oxygenation and maintain normocapnea (PaCO₂ 35–40 mm Hg); hypoxia (PaO₂ < 80%) and hypocapnia (ETCO₂ < 27) from onset of trauma significantly increases mortality (J *Trauma*. 1996;40:764; J *Trauma*. 2004;57:1)
- Maintain SBP > 90 mm Hg; even a single episode of SBP < 90 mm Hg can double mortality and worsen morbidity, hypotension is one of the strongest independent predictors of poor outcome in TBI (*J Trauma*. 1993;34:216)
- Resuscitation with hypertonic saline shown to improve survival compared to isotonic fluids (*Arch Surg.* 1993;128:1003); use crystalloid and avoid albumin, which is associated with higher rates of mortality in severe TBI (*NEJM.* 2007;357:874)
- Treat hypertension (SBP > 180) with beta-blockers or agents that do not dilate cerebral vasculature (e.g., nitroprusside, hydralazine) given potential contribution to increased intracranial pressure (ICP)
- Minimize deleterious effects of brain swelling by avoiding hyponatremia
- Perform trauma survey: TBI is associated with extracranial injury in 35% of cases (*J* Trauma. 1989;29:1193). Immobilize C-spine, assess for fractures. Rule out internal bleeding and other associated injuries.
- Minimize risk for ongoing bleeding by discontinuing and reversing any anticoagulants with goal INR ≤ 1.3 and PTT ≤ 40
- In patients with GCS \leq 8, place ICP monitor and consider intubation
- Seizure prophylaxis in the first 7 days following injury reduces risk of post-traumatic seizures in patients with supratentorial hemorrhages

Neuro-imaging

Obtain a non-contrast CT of head promptly to assess for operative lesions. CT is the initial imaging of choice due to speed, accessibility, and sensitivity for hemorrhage and fractures.

- Consider CT or MR Venogram if a displaced skull fracture is adjacent to venous sinus to assess for potential sinus thrombosis
- MRI is more sensitive than CT for microhemorrhages and DAI but should be delayed until the subacute period when patient is clinically stable and intracranial hypertension has been ruled out, given risk for elevated ICP with prolonged supine position
- CT findings of concern include midline shift >5 mm, extra-axial hematoma thickness >1 cm,

- effacement of basal cisterns, and pneumocephalus (sign of CSF leak)
- Need for surgical intervention depends on neurologic condition of patient, amount of blood, and risk of compromise in the absence of evacuation

Types of Primary TBIs and Their Initial Management Skull Fractures

- Skull fractures may occur independently of or be associated with underlying epidural hematomas or contusions
- Anterior skull fractures may manifest with peri-orbital bruising, or Raccoon eye sign, and CSF rhinorrhea (damage of the cribiform plate)
- Temporal skull fracture may result in post-auricular bruising, known as Battle's sign, CSF otorrhea, and hemotypanum; dedicated temporal bone imaging and possible ENT consult should be considered with the latter signs
- CSF leak poses risk for CSF infection and meningitis; confirm CSF leak by ring test (assess for halo effect of leakage on filter paper), glucose level (mucus usually does not contain significant glucose as opposed to CSF), and quantifying beta-2-transferrin level (may take several days before confirmatory results return); initiate antibiotics if suspicious for CSF leak; placement of lumbar drain offers CSF diversion to encourage spontaneous closure of leak site
- Pneumocephalus in the setting of skull fracture also raises concern for CSF leak
- Cranial nerve palsies may be associated with base of skull fractures, resulting in anosmia (CN I from cribiform plate fracture), diplopia or dysconjugate gaze (CN III, IV, VI from orbital fracture or cavernous sinus injury), facial palsy or hearing loss (CN VII–VIII from petrous temporal bone fracture)
- Significant scleral injection, pulsating exophthalmos, and retro-orbital bruit may suggest a direct or indirect carotid-cavernous fistula, which should be further evaluated by cerebral angiogram

Epidural Hematomas

- Result from injury to the middle meningeal artery (most commonly), middle meningeal vein, diploic veins, or dural sinuses; may be associated with overlying skull fractures
- May present with headache, loss of consciousness with or without lucid interval for several hours, hemiparesis, dilated pupils, or seizure
- CT scan shows extra-axial, hyperdense, biconvex lesion confined by cranial sutures
- Epidural hematomas should be evacuated if larger than 30 cm³, in comatose patients with anisocoria, or in the posterior fossa with compression of the 4th ventricle
- Patients with epidural hematomas smaller than 30 cm³, and less than <15 mm in maximal thickness, with, midline shift <5 mm, GCS > 8, and no focal neurologic deficit may be monitored with frequent neurologic exam and serial CT scans (*Neurosurgery*. 2006;58:S7)
- Poor prognosis has been associated with low GCS on presentation, older age, absence of a lucid interval, bilateral pupil dilatation, associated subarachnoid or intracerebral hemorrhage, and postoperative intracranial hypertension

Subdural Hematomas (see Figure 42.11)

- Result from tearing of bridging veins or extension of large parenchymal hematoma
- May be preceded by minor or no trauma in elderly patients, especially if the patient is anticoagulated
- CT scan shows extra-axial crescentic lesion that can cross cranial suture lines; density on CT depends on acute (<3 d), subacute (<2–3 wks), or chronic (3 wk–3 mo) state

- Acute subdural hematoma >10 mm in thickness or >5 mm in midline shift should be surgically evacuated regardless of GCS (*Neurosurgery*. 2006;58:S16)
- Acute subdural hematomas in patient with GCS \leq 8 should be evacuated if GCS drops by 2 points from time of injury to admission, finding of anisocoria or fixed and dilated pupils, or ICP > 20 mm Hg (*Neurosurgery*. 2006;58:S16)
- Emergent craniectomy or craniotomy for evacuation of acute subdural hematoma within 4 hrs of injury significantly improves mortality rate (*JAMA*. 1981;304:1511)
- ICP control following evacuation of hematoma significantly improves functional recovery (*J Neurosurg.* 1991;74:212)
- Subdural collections liquefy after 2 wks and may be drained by burr holes instead of craniotomy at that point; burr hole drainage may be limited by membranes compartmentalizing clot but may lead to better functional status than craniotomy (*J Neurosurg*. 1964;21:172)
- Following subdural hematoma evacuation, if postoperative CT scan reveals sunken brain with pneumocephalus, maintain bed rest with head of bed flat and 100% oxygen supplementation for 24 hrs to reduce risk of recurrence
- Differentiate from subdural hygroma resulting from intracranial hypotension to prevent unnecessary surgical intervention
- Poor prognosis is associated with age >65, low GCS on presentation, delay in surgical intervention if acute, and postoperative intracranial hypertension

Cerebral Contusions and Intraparenchymal Hematomas

- Occur at sites where the brain strikes prominent bony margins, most commonly, the inferior anterior frontal lobe and anterior temporal lobe
- May occur on contralateral aspects of cerebral hemispheres from direct impact followed by rebound against cranium, or coup and contracoup injury; found in 25%–35% of severe TBI cases, with significant risk for expansion and mass effect
- Repeat CT scan of head within 6 hrs after initial scan to assess for evolution of contusion, or sooner if signs of clinical deterioration or significant coagulopathy; may blossom over the course of days, mandating close serial monitoring
- Risk factors for enlarging contusions include: large size of initial lesion, presence of SDH or EDH, older age, and elevated PTT
- Mechanisms include shearing of intraparenchymal vessels at the time of injury or subsequent coagulopathy (from traumatic release of thromboplastin following brain injury), vascular necrosis, hyperperfusion injury from impaired cerebrovascular autoregulation, and release of tamponade effect after evacuation of extra-axial hematoma
- Temporal lobe contusions and hemorrhages may cause compartmentalized intracranial hypertension with resultant uncal herniation despite seemingly normal ICPs from parenchymal or intraventricular pressure monitors
- Consider surgical evacuation for hematomas >50 cm³ or temporal hematomas >20 cm³ with compression of basal cisterns and impending uncal herniation (*Neurosurgery*. 2006;58:S25)
- Early evacuation of traumatic intraparenchymal hematomas did not improve outcomes over medical management, but may be offered to young patients with small and superficially located lobar clots (STICH: *Lancet*. 2005;365:387)
- Decompressive craniectomy may be indicated in patients <60 yrs of age with medically refractory intracranial hypertension and malignant edema, with diligent monitoring for and control of potential associated complications, including post-operative subdural and epidural hematomas, infections

and hydrocephalus. A recent trial suggested that bifrontotemporoparietal decompressive craniectomy compared to maximal medical management for diffuse traumatic brain injury decreased ICP and ICU stay, but was associated with worse functional outcome, and no diffuse in mortality (DECRA: *NEJM*. 2011;364:1493); however, the study population excluded patients with mass lesions and dilated unreactive pupils, which comprise a significant portion of potential candidates, and also used a surgical approach that differs from the unilateral hemicraniectomy utilized at many institutions. Overall, systemic evidence for benefits of decompressive craniectomy in adults with severe head trauma remains lacking (*Cochrane review*, 2009)

Diffuse Axonal Injury

- Associated with poor prognosis
- Manifests as small hyperdensities on noncontrast CT scan if hemorrhagic, or hyperintensity on DWI or T2-weighted MRI if non-hemorrhagic; diffusion tensor imaging offers more sensitive evaluation of DAI, if available
- Vulnerable regions include corpus callosum (especially splenium), corona radiata (especially greywhite junction), internal capsule, midbrain, and dorsolateral pons
- Corpus callosum DAI may be associated with intraventricular hemorrhage due to disruption of subependymal venous plexus along ventricular surface of corpus callosum (AJNR. 1988;9:1129)

Subarachnoid Hemorrhage (see Figure 42.10)

- Occurs typically within cortical sulci, in the cerebral convexities rather than in basal cisterns
- Low risk of subsequent vasospasm and cerebral salt wasting, in contrast to subarachnoid hemorrhage from aneurysm rupture

Duret Hemorrhage

• Occurs in ventral or paramedian brainstem due to shearing of perforating arteries with transtentorial herniation; may occur in delayed fashion

Secondary Brain Injury

- Results from evolution of primary injury processes, hypotension, hypoxia, intracranial hypertension, and inadequate cerebral perfusion pressure (CPP)
- Mechanisms include expansion of contusion or hematoma, excitotoxic neurotransmitter release, altered mitochondrial metabolism, free radical and calcium-mediated injury, blood-brain barrier disruption from mechanical injury and inflammatory cytokine release, increased extracellular potassium, and alterations in gene expression with increased production of pro-apototic factors
- Leads to intracranial hypertension and cerebral ischemia

Intracranial Pressure

- Monro-Kellie doctrine: the cranial vault is comprised of brain parenchyma, cerebrospinal fluid, and arterial and venous blood. Any single compartment can only increase at the expense of compression of the remainder compartments
 - Some buffering capacity exists from: compression of venous sinuses, caudal displacement of CSF
 - Further \(\) volume causes \(\) ICP given a steep intracranial compliance curve
 - \uparrow ICP $\rightarrow \downarrow$ cerebral perfusion or herniation
- Normal ICP is ≤15–20 mm Hg in adults; sustained ICP ≥ 20 mm Hg correlates with worse outcome and higher mortality risk
- Cushing's response to intracranial hypertension: hypertension, bradycardia, irregular respirations
 - \uparrow ICP $\rightarrow \uparrow$ sympathetic response $\rightarrow \uparrow$ systemic vascular resistance $\rightarrow \uparrow$ MAP (hypertension) \rightarrow

reflex compensatory response (bradycardia) \rightarrow cerebral vasodilation \rightarrow further \uparrow ICP (Cheyne-Stokes respiration)

Cerebral Perfusion

- Cerebral blood flow (CBF) and oxygenation are critical for brain viability, but is difficult to measure; CPP is often used as an indirect surrogate for CBF
 - CBF = CPP/CVR (CVR = cerebral vascular resistance)
 - CPP = MAP ICP (Normal CPP > 50 mm Hg)
- Normal CBF = 50-55 cc/100 g brain tissue/min; CBF ischemic threshold = 18-20 cc/100 g/min; CBF < 10 cc/100 g brain tissue/min leads to irreversible neuronal injury
- CBF remains constant between CPP 50 and 150 mm Hg (or MAP 60 and 160 mm Hg if ICP normal) due to auto-regulatory mechanisms; beyond this range, CBF becomes pressure-dependent
 - \downarrow CPP \rightarrow arteriole dilatation, \downarrow CVR $\rightarrow \uparrow$ CBF \rightarrow potentially \uparrow ICP $\rightarrow \downarrow$ CPP
 - $\uparrow \uparrow$ CPP (>150 mm Hg) \rightarrow maximal arteriole dilation $\rightarrow \uparrow$ CBP $\rightarrow \uparrow$ ICP
- In TBI, auto-regulation may be impaired with CPP < 50 mm Hg, lowering the threshold for ischemic injury. Maintaining CPP between 50–70 mm Hg can reduce mortality by 50% in severe TBI, while driving CPP > 70 mm Hg increases the risk of ARDS by five-fold (*Crit Care Med.* 1999;27:2086)
- CBF correlates with $PaCO_2$ but not PaO_2 : every 1 mm Hg change in $PaCO_2 \rightarrow 3-4\%$ change in cerebral vascular lumen; $\uparrow PaCO_2$ vasodilates, $\downarrow PaCO_2$ vasoconstricts
- Cerebral oxygenation is optimized by $PaO_2 > 60 \text{ mm Hg}$, SBP > 90 mm Hg, and hematocrit ≥ 30 ; compare brain injury with cardiac ischemia in oxygenation demands
- Alterations in cerebrovascular autoregulation predict worse outcome (*J Neurosurg.* 2006;104:731)

Intracranial Pressure Monitoring

- ICP monitor should be placed in TBI patients with GCS ≤ 8 and an abnormal brain CT, or with a normal brain CT but who are >40 yrs old, have SBP < 90 mm Hg, or exhibit motor posturing (*J Neurotrauma*. 2007;24:S37)
- Types of ICP monitors:
 - External ventricular drain (EVD): effectively monitors as well as reduces ICP through CSF drainage; most commonly placed into frontal horn of lateral ventricle with distal tip at the foramen of Monroe, which correlates to level of the tragus for calibration of drain pressure; more accurate than parenchymal monitors and has significant advantage of therapeutic CSF drainage in addition to ICP monitoring
 - Intraparenchymal monitor: option when CSF drainage considered unnecessary or severely compressed ventricular space which prevents facile insertion of EVD; may miss compartmentalized intracranial hypertension, as seen with temporal contusions; increased infection risk and decreased accuracy after 3 days
 - Subarachnoid bolt: option in coagulopathic patients; less accurate than intraventricular and intraparenchymal monitors; decreased accuracy with high ICP; increased infection risk after 3 days
- Duration of monitoring: onset of intracranial hypertension peaks at day 2–3 and day 9–11; continue monitoring until ICP therapy is weaned
- Reverse coagulopathy prior to placement; common practice to give prophylactic antibiotics although evidence remains controversial as to its impact on reducing infections

- ICP interpretation: normal ICP waveform varies with respiration and blood flow, but may be distorted in TBI due to intracranial hypertension or craniectomy skull defect
- Cessation of CSF drainage from EVD may be due to:
 - Low ICP
 - Malposition of EVD out of CSF space
 - Catheter occlusion: assess patency by lowering the external monitor; if no distal CSF flow is visualized, the EVD tubing may be flushed with a small volume of sterile saline
 - Filter paper on top of external collection system becomes wet, often when the system is disassembled from hanging position for patient transport; the external system can be replaced in sterile fashion without replacement of intraventricular catheter

Management of Intracranial Hypertension

Elevated ICPs, both sustained and reversible, predicts poor neurologic outcome. If \uparrow ICP is suspected, obtain initial non-contrast CT scan of head immediately. Multiple measures exist to maintain ICP < 20 mm Hg and optimize CBF.

- Maximize venous drainage: elevate head to 30 degree; further elevation of head risks compromising CPP and CBF; prevent over-constriction from any cervical collar or tracheostomy restraints
- Normocapnia: goal PaCO₂ 35 mm Hg; \downarrow CO₂ \rightarrow \downarrow CBF \rightarrow \downarrow ICP within 30 secs, sustained effect for <1 hr, with risk of rebound \uparrow ICP when CO₂ normalizes
 - Prolonged prophylactic hyperventilation (PaCO₂ 24–28) is associated with significantly worse outcome than normoventilation (PaCO₂ 30–35) in severe TBI patients (*J Neurosurg*. 1991;75:731)
 - Avoid in initial 24 hrs following TBI
 - Consider brief hyperventilation to PaCO₂ 30–35 as temporizing measure in patients with acute neurologic deterioration and impending herniation, until other treatments can be implemented
 - Consider monitoring jugular bulb venous saturation (SjVO₂), brain tissue oxygen tension (PBtO₂), or CBF during hyperventilation for potential cerebral ischemia
 - Mild chronic hyperventilation may be indicated for \(\gamma\) ICP due to cerebral hyperemia, which can result from rapid decompression of chronic subdural hematomas in elderly pts
 - Positive pressure support may exacerbate ICP, although the relationship between PEEP and ICP is unpredictable
- Sedation: propofol and short-acting narcotics (e.g., fentanyl) may decrease ICP by controlling sympathetic stimuli; neuromuscular blockage is a further adjunct for refractory severe ICP elevations
 - Propofol can cause vasodilation; monitor for hypertriglyceridemia and pancreatitis with prolonged use
- CSF drainage: EVD effectively monitors as well as reduces ICP with instantaneous effect; recommend in all possible cases prior and in addition to hyperosmolar therapy
- Hyperosmolar therapy: mannitol and hypertonic saline are mainstays of ICP reduction, associated with improved clinical outcome in select populations of TBI pts
 - Mannitol: 1–1.5 g/kg bolus over 30–60 min followed by 0.25–0.5 g/kg q6h for ↑ ICP; scheduled empiric mannitol dosing shown to ↓ ICP more than reactive administration of mannitol in response to ↑ ICP, although may not alter mortality risk (*J Neurosurg*. 1986;65:820)
 - Monitor serum Na, Osm, BUN, Cr; hold if serum osmolarity >320 mOsm/l or osmolar gap >11

- Risks: rebound intracranial hypertension, renal failure, hypotension, or hypertension with prolonged use
- Mechanisms of action: osmotic diuresis, plasma expansion, decrease blood viscosity, free radical scavenging
- Hypertonic saline: 30–60 ml of 23.4% over 20 min is effective alternative to mannitol; 3% and 7.5% NaCl also candidates to \$\perp\$ ICP
 - Recommend: bolus 23.4% NaCl through central venous line, then maintain hypernatremia with 3% infusion at 20–60 ml/hr through peripheral IV
 - Monitor serum Na, Osm, BUN, Cr; hold if Na > 160 mEq/l, serum osmolarity >320 mOsm/l
 - Risks: central pontine myelinosis, seizures, hypernatremia, CHF, coagulopathy; lower risk of rebound intracranial hypertension and renal failure compared to mannitol
 - Mechanisms of action: osmotic diuresis, anti-inflammatory effect
- Decompressive craniectomy: removal of cranial vault and expansion of dura over affected hemisphere, with possible resection of contused brain parenchyma, may augment ICP control in those pts with intracranial hypertension refractory to aggressive medical management, although its impact on functional outcome remains unclear, possibly due to associated complications of this procedure (DECRA: *NEJM*. 2011;364:1493). Further randomized multi-institutional trial is currently underway and may give a more definitive answer on functional impact of craniectomy.
- Barbiturates: consider in pts with persistent \(\) ICP refractory to all preceding medical management and surgical compression; unclear impact on outcome (*J Neurosurg.* 1988; 69:15)
 - Consider pentobarbital 10 mg/kg IV over 30 min, then 5 mg/kg q1h × 3 doses, then 1 mg/kg/hr
 - Monitor burst suppression with continuous EEG and hemodynamics with Swan-Ganz catheter
 - Risks: hypotension, oligemic hypoxemia, hypokalemia, respiratory depression, paralytic ileus, hepatic injury, renal injury, loss of neurologic exam, confounds brain death exam
- Hypothermia: controversial as to whether prophylactic cooling to 32–35 degree improves outcome in severe TBI; does not improve mortality rate (*NEJM*. 2001;344:556; *J Neurotrauma*. 2007;24:S21)
- Steroids: not recommended for cytotoxic cerebral edema in TBI; increased mortality risk

Consequences of Intracranial Hypertension

- Hydrocephalus: place EVD for CSF diversion
- Cerebral ischemia
- Herniation:
 - Uncal herniation: medial displacement of the temporal lobe (uncus and hippocampal gyrus), causing midbrain compression and consequent ipsilateral fixed and dilated pupil, contralateral hemiparesis, and altered mental status with eventual coma
 - Ipsilateral hemiparesis can result from compressing the contralateral cerebral peduncle against the tentorial incisura (Kernohan's notch)
 - Imaging demonstrates: effacement of suprasellar and perimesencephalic cisterns, medial dislocation of the temporal horn of lateral ventricle, and unilateral compression of cerebral peduncle
 - Central diencephalic herniation: caudal displacement of diencephalon from bilateral supratentorial hypertension, causing altered consciousness, decreased motor response, abnormal eye movements, and eventual bilateral fixed and dilated pupils
 - Lethargy or agitation is the first sign of central herniation, while pupillary changes are a late

finding, in contrast to uncal herniation

- Impingement of posterior cerebral arteries can lead to occipital infarcts
- Stretch of the pituitary infundibulum may result in diabetes insipidus
- Imaging demonstrates: effacement of perimesencephalic cisterns, Duret hemorrhages
- Tonsillar herniation: caudal displacement of cerebellum by increased pressure in the posterior fossa, leading to medullary compromise and coma
 - Classically associated with Cushing's triad (hypertension, bradycardia, respiratory irregularity)
 - Imaging demonstrates: tonsillar descent through the foramen magnum, diffuse hydrocephalus
- Subfalcine herniation: lateral displacement of cingulate gyrus under falx, which may compress the anterior cerebral arteries and lead to lower extremity paresis; may precede central herniation
- Mortality

Sympathetic Storms

- Episodic hypertension, tachycardia, tachypnea, hyperthermia, diaphoresis, pupillary dilation, and flexor–extensor posturing observed in severe TBI pts
- Onset can occur within hrs to weeks after injury; periodicity of minutes to hrs
- May be precipitated by discontinuation of sedatives, such as following extubation of critically ill pts, and tactile stimuli
- May be confused for infectious state given persistent fever or catecholamine-secreting mass
- Diagnosis of exclusion: rule out underlying etiologies with pan-cultures, laboratory workup, and imaging, but clinical history and periodic nature of syndrome strongly suggests autonomic dysregulation
- Treatment: narcotic analgesia, bromocriptine, clonidine, propranolol, labetalol
 - Recommend: morphine sulfate q4h and bromocriptine 2.5–5 mg q4–8h, followed by trial of clonidine 0.1–0.2 mg BID

SPINAL CORD INJURY

Neurological Assessment

• Physical exam should include assessment of key muscle groups, sensory levels, deep tendon reflexes, rectal exam, and the bulbocavernosous reflex, as well as palpation of the spine

	Key Muscle Groups to	Assess in Spin	al Cord Injury (SCI)
C5	Elbow flexors	L2	Hip flexors
C6	Wrist extensors	L3	Knee extensors
C7	Elbow extensors	L4	Ankle dorsiflexors
C8	Finger flexors	L5	Long toe extensors
T1	Finger abductors	S1	Ankle plantar flexors

Adapted from: American Spinal Injury Association classification of spinal cord injury.

- Neurologic deficit, even if transient, in the setting of a high-energy mechanism suggests an unstable spine
- Complete spinal cord injury refers to absence of any motor or sensory function below the level of injury, including in S4–S5. This should be distinguished from incomplete SCI to guide management and prognosis, as long as the patient is not in spinal shock

- Incomplete injury requires perianal sensation or voluntary rectal tone, as opposed to involuntary tone, which may be partially preserved in complete SCI
- Presume SCI in trauma patients until proven otherwise
- Spinal shock:
 - Suppression of spinal cord reflex activity in the early phase of acute spinal cord injury
 - Confounds distinction between complete versus incomplete spinal cord injury during period of spinal shock, most common within the first 24 hrs
 - Distinguish by assessing the bulbocavernosus reflex, presence of which excludes spinal shock
- Neurogenic shock:
 - Triad of hypotension, normal to bradycardia, and hypothermia
 - Results from a temporary functional loss of sympathetic tone and inability to mount reflex response; unopposed parasympathetics lead to vasodilation, decreased cardiac output, and hypotension
 - Usually seen in cervical or upper thoracic cord injury
 - Avoid aggressive fluid resuscitation, as in the treatment of hemorrhagic shock, to prevent fluid overload and pulmonary edema
 - Manage with β-agonists, a-agonists, or anticholinergies to improve cardiac output

	Spinal Cord Injury Classification
	ASIA Impairment Scale
ASIA A	Complete injury. No motor or sensory function below the level of injury, including in the sacral segments S4-S5.
ASIA B	Incomplete injury. Sensory but not motor function is preserved below the level of injury, including the sacral segments S4-S5.
ASIA C	Incomplete injury. Motor function is preserved below the level of injury, with more than half of the muscles below the level of injury with grade <3 in strength.
ASIA D	Incomplete injury. Motor function is preserved below the level of injury, with at least half of the muscles below the level of injury with grade 3 or more in strength.
ASIA E	Normal. Intact motor and sensory function.

Adapted from: American Spinal Injury Association (ASIA) classification of spinal cord injury.

Incomplete Spinal Cord Injury Syndromes

- Central cord syndrome:
 - Mechanism: hyperextension injury, especially in elderly pts with pre-existing spinal stenosis
 - *Presentation*: bilateral weakness with upper extremities affected more than lower extremities; bilateral sensory deficits; upper extremity hyporeflexia, lower extremity hyperreflexia; urinary retention
 - *Prognosis*: partial recovery may be expected, especially of the lower extremities and bowel and bladder; half of patients with cord contusion without hematomyelia regain ambulatory capacity; recovery of fine motor hand function is less frequently observed
- Brown–Sequard syndrome:
 - *Mechanism*: hemisection of the spinal cord; may result from penetrating trauma, lateralized disc herniation, epidural hematoma, tumors, and AVMs
 - *Presentation*: ipsilateral paralysis and loss of proprioception with contralateral loss of pain and temperature sensation below the level of injury, preserved sensation of light touch

- Prognosis: favorable, 90% of pts recover ambulation and bowel and bladder function
- Anterior cord syndrome:
 - Mechanism: anterior spinal artery compromise, retropulsion of fractured vertebral body
 - *Presentation*: bilateral weakness and loss of pain and temperature sensation below the level of injury
 - Prognosis: poor, few regain motor function
- Posterior cord syndrome:
 - Mechanism: B12 deficiency, tertiary syphilis
 - *Presentation*: loss of deep pressure sensation and proprioception, intact motor function, intact pain and temperature sensation, foot slapping gait
 - Prognosis: favorable, treat the underlying disease
- Cauda equina syndrome:
 - *Mechanism*: compression of caudal equina by lumbar disc herniation, tumor, hematoma, abscess, or trauma
 - *Presentation*: saddle anesthesia, weakness involving multiple nerve root, paraplegia, urinary retention or incontinence, sciatica
 - Prognosis: dependent on timing before decompression

Radiographic Evaluation of Spinal Cord Injury

- Imaging of the spine should be obtained in prompt fashion
 - X-rays of the cervical spine should include AP, Lateral, and possibly open-mouth views. An adequate x-ray must visualize the occiput through the cervical—thoracic junction. However, CT scans have largely replaced plain films in spinal evaluation.
 - Stability of the occipital—cervical junction can be suggested through a number of radiographic measurements, including the basion-dental interval (BDI), basion-posterior axial line interval (BAI), Power ratio (basion-C1 arch/tip of dens-opisthion distance), Chamberlain's line (posterior tip of the hard palate to opisthion), Wackenheim's line (clivus to odontoid), and McCrae's line (basion to opisthion)
 - Of the various measures suggesting occipital—cervical junction instability, the BDI and BAI, which fall within 12 mm in normal subjects, may have the highest reproducibility in acute spine trauma (*Spine*. 2007;32:593)
 - Stability of C1 lateral mass fractures is suggested by the rule of Spence, which states that the sum of bilateral lateral mass overhang should be <7 mm
 - C1–C2 stability is often marked by the atlantodens interval (ADI), the calculated space between the posterior surface of the atlas and the anterior surface of the dens, which falls within 3.5 mm in adults. Increased ADI suggests injury to the transverse ligament and decreased stability
 - C2–C3 traumatic spondylolisthesis, or Hangman's fractures, is marked by the distance of anterior-posterior displacement and degree of angulation (*J Bone Joint Surg Am.* 1985;67:217)
 - CT scan entire cervical, thoracic, and lumbar spine in trauma patients given propensity for multilevel injury
 - MRI should be performed for patients with neurologic deterioration, neurologic deficits not accounted for by degree of bony injury, and to assess for ligamentous injury. MRI is considered most useful in the initial 48 hrs following spinal cord trauma
 - Flexion–extension views of the cervical spine may be useful as an alternative to MRI to assess for ligamentous laxity; they should be avoided in obtunded patients in the acute setting and in patients

with fractures that may be unstable

- Cervical spine may be clinical cleared without imaging if patient with minor trauma fulfills NEXUS criteria (*NEJM*. 2000;343:94):
 - Alert and oriented patient
 - Intact neurologic status
 - Absence of midline posterior cervical spine tenderness on palpation
 - Absence of other painful injuries which may distract the patient from neck injury
- Clearance of the cervical spine in unresponsive patients may be made if a combination of CT scan and either MRI or physician-guided flexion-extension x-rays of the cervical spine are negative for injury
- Be cautious for spinal cord injury without radiographic abnormality (SCIWORA), especially common in children

Initial Management of Spinal Cord Injury

- Maintain patients with suspected SCI in cervical collars until radiographically or clinically cleared; maintain log-roll precautions in thoracolumbar SCI patients until surgical or external brace stabilization
 - Remove cervical collar as soon as possible to reduce ICP and pressure ulcer risk
- Maintain MAP goal 85–100 in the first 7 d following injury to prevent secondary cord injury due to hypoperfusion; avoid hypotension (SBP < 90 mm Hg)
 - Consider neurogenic shock if hypotension with bradycardia, use vasopressor rather than aggressive hydration
 - Dopamine is vasopressor of choice to minimize risk of reflex bradycardia
- Closely monitor respiratory status and ABG; assess vital capacity when stable;
 - High risk for aspiration and respiratory failure in cervical SCI
 - Intubate if signs of hypoxia, hypercarbia, decreasing vital capacity, or poor mental status
 - Perform early tracheotomy in patients likely to remain ventilator dependent
 - Stress ulcer prophylaxis should be given if patient is intubated
 - Treat retained secretions due to expiratory muscle weakness with manually assisted coughing, mechanical insufflation—exsufflation, or other expiratory aids in addition to suctioning
- Make patients NPO upon presentation; place NG/OG tube if somnolent or intubated given risk for aspiration
 - Stress ulcer prophylaxis (H₂ blocker or PPI) if intubated or on steroids
 - Dysphagia screen prior to oral intake
 - Provide aggressive bowel regimen given propensity for constipation and ileus
- PVR should be measured on presentation; place Foley catheter for patients with significant urinary retention
- Hypothermia remains controversial for acute SCI and is not recommended for TBI

Steroid Therapy

- Controversial for incomplete blunt acute SCI; not indicated in penetrating SCI
- Steroids given to SCI patients within 8 hrs of injury may result in higher motor and sensory scores in long-term (6 mo) follow-up, but also significantly increase risk of infections; steroids are associated with worse prognosis if initiated after 8 hrs from time of injury (*NEJM*. 1990;322:1405; *JAMA*. 1997;277:1597)

- Methylprednisolone IV bolus at 30 mg/kg body weight over 15 min, followed by 45 min pause, then infuse at 5.4 mg/kg/hr for 23 hrs if initiated within 3 hrs of injury or for 47 hrs if initiated within 3 hrs of injury
- Significant controversy over the NASCIS study design and analysis have called into question the validity of its results, with current national guidelines stipulating that any benefits of steroid use may be outweighed by risks of associated infections (*J Spinal Disord*. 2000;13:185)
- Provide stress ulcer and hyperglycemia prophylaxis during steroid administration

Nonsurgical Management of Cervical Spine Injuries

• Consider emergent closed reduction in the setting of spinal column instability, progressive neurologic deficits from known cord compression, and open spine fractures

Emergent Surgical Management

- Indicated in the setting of spinal column instability, progressive neurologic deficits from known cord compression, and open spine fractures
- Not indicated for complete SCI
- Surgery for acute SCI in the absence of instability, cord compression, or progressive deficits is usually acute but may be deferred until presumed swelling abates as in central cord syndrome

Complications and Long-term Management of Spinal Cord Injury

- Autonomic dysreflexia: consider abdominal binder, thigh-high compression stockings, and midodrine for orthostatic hypotension
- Pulmonary infections: aggressive pulmonary toilet and chest PT, frequent turns and assist with cough
- Urinary training: scheduled straight catheter regimen to increase detrusor tone
- Spasticity results from upper motor neuron damage
 - Ankle–foot orthosis and wrist bracing to prevent foot drop and contractures
- Deep vein thrombosis are found in a high proportion of SCI pts
 - Initiate heparin s.c. and pneumatic compression boots and stockings immediately following injury
 - Low threshold for Doppler ultrasound for DVT; if DVT, therapeutically anticoagulate or place IVC filter if contraindications to anticoagulation
- Skin breakdown: monitor for pressure ulcers vigilantly
 - Turn or reposition every 2 hrs for pressure relief, while maintaining spinal precautions
 - Provide air mattress bed for quadriplegics
 - Avoid spinal orthosis when patient is resting in bed

NEUROLOGICAL CRITICAL CARE

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COMA AND DISORDERS OF CONSCIOUSNESS

Coma: a state of unarousable unresponsiveness.

Vegetative State: unawareness of self or environment, but w/ preservation of sleep/wake cycles and complete or partial preservation of hypothalamic and brainstem autonomic functions

Persistent Vegetative State (PVS): >1 mo in vegetative state

Permanent Vegetative State: 3 mos after non-traumatic brain injury, 1 yr after TBI

Minimally Conscious State (MCS): severely impaired consciousness in which minimal but definite behavioral evidence of self-awareness or environmental awareness is demonstrated

Locked-in Syndrome: state of de-efferentation w/ quadriplegia and loss of lower cranial nerve function but preservation of sensation, cognition, and eye mymts

Catatonia: a state of unresponsiveness predicated on a psychiatric disorder w/ disturbance of motor behavior but maintenance of consciousness. Stuporous and hyperexcitable forms of catatonia exist, w/ stuporous form potentially being mistaken for coma. Behavioral disturbances include mutism, posturing, waxy flexibility, and catalepsy.

Coma Scales: multiple coma scales exist; see Chapter 18 for Glasgow Coma Scale (GCS)

Pathophysiology, Differential Diagnosis, and Clinical Manifestations:

Neuroanatomic Localization: dysfn of brainstem reticular activating system, thalamic relay nuclei, and/or b/l diffuse dysfn of cerebral hemispheres. In coma of unknown etiology, subsequently determined causes: diffuse and/or metabolic brain dysfn > supratentorial lesion > psychiatric "coma" (conversion rxn, depression, catatonic stupor)

Etiologies of Coma (Plum and Posner's Diagnosis of Stupor and Coma 2007)

- *Structural Causes* (Compressive/Destructive): *hemispheres* (EDH, SDH, SAH, ICH, stroke, hypoxic ischemic encephalopathy, tumor, abscess, meningitis, encephalitis, vasculitis, leukoencephalopathy, prion dz, progressive multifocal leukoencephalopathy); *Diencephalon* (basal ganglia ICH, stroke, tumor, abscess, pituitary tumor, pineal tumor, encephalitis, fatal familial insomnia, paraneoplastic syndrome); *Brainstem* (cerebellar stroke, ICH, tumor, abscess; brainstem stroke, ICH, tumor, or infxn)
- *Diffuse, Multifocal, or Metabolic Causes*: hypoxia, ischemia, hypoglycemia, vitamin co-factor deficiency: thiamine, niacin, pyridoxine, B12, folate; endogenous metabolic products (hepatic coma, uremic coma, CO₂ narcosis, exocrine pancreatic encephalopathy, myxedema-thyrotoxicosis, hypo- or hyper-parathyroidism, adrenal dz); meds/poisons (sedatives, acidic agents, psychotropic drugs, medication overdose); sepsis, hypo- or hypernatremia, acidosis or alkalosis, hypo- or hyper-Mg, hypo- or hyperCa, hypo-phos, temp dysregulation (hypothermia or heat stroke), seizure or postictal state, concussion, psychogenic.

(Neurology. 2002;58:349)				
	Coma	PVS	MCS	Locked-in Syndrome
Consciousness	None	None	Partial	Full
Sleep/Wake	Absent	Present	Present	Present
Motor Function	Reflex and Postural	Postures or w/d to noxious stim; occ nonpurposeful mvmt	Localizes; reaches for and holds objects; automatic mvmts, e.g., scratch- ing	Quadriplegic
Auditory Function	None	Startle; briefly orients to sound	Localizes to sound location; inconsis- tent following of verbal commands	Preserved
Visual Function	None	Startle; brief visual fixation	Sustained visual fixation and visual pursuit	Preserved
Communication	None	None	Contingent vocaliza- tion; inconsistent but intelligible verbalization or gesture	Aphonic and anarthric; blink- ing and vertical eye mvmts usually intact
Emotion	None	May have reflexive crying or smiling	Contingent crying or smiling	Preserved

Initial Management and Evaluation of Coma and Impaired Consciousness:

ABCs, 1 gm/kg IV dextrose, 1 mg/kg IV thiamine, 0.01 mg/kg IV naloxone

Comprehensive metabolic panel, CBC w/ diff, coags, ABG/VBG, serum and urine tox screen, serum osms, EKG; consider TFTs, adrenal function tests, UA/UCx, Bld Cxs

Head CT and/or brain MRI. Consider LP, EEG

Additional laboratory and imaging investigations based on clinical suspicion for specific etiology.

Prognosis of Coma, PVS and MCS: coma prognosis varies widely depending on underlying cause. Post-TBI coma has better outcomes than post-anoxia coma.

Prolonged coma rare; most progress to PVS w/in 1 mo. Both PVS and MCS can exist as permanent or transitional states. Likelihood of significant fxnl improvement \(\psi \) s over time for both PVS and MCS.

BRAIN DEATH

Definition of Brain Death: total and irreversible cessation of all spontaneous and reflexive brain functions. Brain death is clinically determined by coma, absence of brain stem reflexes, and apnea. Ancillary testing not necessary in adults, but may be used for determination of brain death when clinical testing is limited or questionable (*NEJM*. 2001;344:1215)

Preparation for Brain Death Assessment: (1) Notify local organ bank. (2) Involve pt's nurse and if appropriate, religious officials and/or medical ethics services before discussing plans for brain death assessment w/ family. (3) Discontinue sedatives or hypnotics. (4) Confirm that the following clinical criteria are met: known and irreversible cause of neurological injury; Clinical or radiologic evidence of CNS catastrophe consistent w/ brain death; If cardiac arrest is the etiology, consider observing >6

hr then re-examining; No severe acid/base, electrolyte, endocrinologic disturbances or hyperammonemia; No drug/EtOH intoxication (if barbiturates levels present, must be <10 mcg/ml or "absent" on tox screen); if significant doses of CNS depressants have been administered recently, use ancillary testing; No neuromuscular blockade (if pt recently received neuromuscular blocking agents, must confirm reversal w/ train-of-four stimulation); If severe facial trauma, prior pupillary abnormalities, toxic levels of sedative drugs, or severe chronic CO_2 retention limit the clinical assessment of brain death, use ancillary testing.

Clinical Findings Consistent w/ Brain Death: facial myokymias; Spontaneous spinal mymts of limbs [not decerebrate/decorticate posturing (*Neurol*. 1984;34:1089)]; Respiratory-like mymts: shoulder elevation/adduction, back arching, intercostal expansion w/o significant tidal vol; Sweating, blushing, tachycardia; Normal osmolar control mechanisms (absence of diabetes insipidus); Presence of DTR's, triple flexion

Clinical Findings that Preclude Brain Death: decerebrate or decorticate posturing of the limbs; Pinpoint pupils → must rule out narcotic overdose; Spontaneous breathing mymts.

Clinical Criteria for Brain Death

- Coma: no eye opening, verbal response, or purposeful mvmt. No purposeful withdrawal to noxious stim w/ supraorbital pressure and nail-bed pressure in all 4 extremities.
- Absence of brainstem reflexes: Pupils: fixed pupils, even w/ bright light and magnifying glass; Ocular Mvmts: no oculocephalic reflex → only test if C-spine integrity has been ensured; No oculovestibular reflex (absent caloric stimulation response) → confirm integrity or tympanic membrane and absence of significant blood/cerumen in external auditory canal, elevate head-of-bed to 30 degrees and irrigate external auditory canal w/ 30–50 ml of ice-water; observe for ocular response (1 min); repeat on contralateral side after at >5 min delay. Facial Motor Responses: no corneal reflex to touch w/ cotton swab. No facial grimace to deep pressure on nailbeds, supraorbital ridge, or temporomandibular joint. Pharyngeal and Tracheal Reflexes: no gag w/ stimulation of posterior pharynx. No cough to bronchial suctioning.
- Apnea testing: prerequisites and preparation: core Temp ≥ 36.5 °C (96.8°F). SBP $\geq 90 \rightarrow \text{if pt}$ requiring pressors or experiencing arrhythmias, consider ancillary testing instead of proceeding w/ apnea test. Euvolemia → if diabetes insipidus present, need + fluid balance over prior 6 hrs. Adjust ventilator settings to achieve arterial pH 7.35–7.45 and PaCO₂ 35–45 mm Hg ≥20 min prior to apnea testing (or to pt's baseline, if known CO_2 retainer). Pre-oxygenate w/ 100% FiO_2 for 5 min to $PaO_2 > 200$ mm Hg. Procedure: disconnect pt from ventilator. Administer 100% O_2 at 8–10 1/min via endotracheal tube or tracheostomy to level of carina immediately after disconnecting vent. Observe for respiratory mymts for approximately $8 \text{ min} \rightarrow \text{abdominal or chest excursions}$. After 8 min period elapses, check ABG to measure PaO₂, PaCO₂, and pH. Reconnect pt to ventilator after ABG is drawn. If during 8 min period off ventilator, pt develops cyanosis, SBP < 90 mm Hg, significant O_2 desaturation, or cardiac arrhythmia \rightarrow draw STAT ABG, discontinue apnea testing and reconnect ventilator. Positive Apnea Test (consistent w/ Brain Death): no respiratory mvmts. ABG Criteria: $PaCO_2 \ge 60 \text{ mm Hg or } PaCO_2 \text{ increase } \ge 20 \text{ mm Hg from}$ baseline. Apnea test considered positive if stopped early as long as no respiratory mymts are observed and ABG criteria are met. Negative Apnea Test: respiratory mymts observed OR ABG criteria not met after sufficient time elapsed. Indeterminate Apnea Test: apnea test performed, w/

no respiratory mvmts observed but ABG criteria not met → may repeat test for longer time period

if clinically stable, or proceed to ancillary testing.

	Ancillary Testing to Confirm Brain Death
Diagnostic Test	Findings Consistent w/ Brain Death
EEG	Core Temp must be ≥36.5°C (96.8°F) No EEG activity for ≥30 min No change in EEG record w/ auditory, visual or noxious stimulation EEG interpretation must be confirmed by attending neurologist
4-Vessel Angiogram	No contrast filling of cerebral vasculature in anterior or posterior circulation Contrast filling of ICAs should stop abruptly at petrous segment where ICA becomes intracranial Delayed filling of superior sagittal sinus may be seen due to patency of external carotid circulation
SPECT w/Tech 99	No uptake of isotope in brain parenchyma → study must be interpreted by attending nuclear medicine physician Isotope uptake w/in meninges and skull vessels may be seen due to perfusion from external carotids
Transcranial Doppler (TCD)	Perform TCD cerebral blood flow velocity measurements in b/l intracranial cerebral vasculature and extracranial vasculature (CCAs, ICAs, cervical portions of vertebral arteries) Must observe small systolic peaks in early systole w/o diastolic flow or w/ reverberating flow → suggests high vascular resistance from increased ICP and absence of tissue blood flow TCDs must be performed 2x, 30 min apart

Documentation of Brain Death in Medical Record: date and time of death (for ancillary testing, use time of interpretation), name the physician declaring brain death, etiology and irreversibility of neurological injury, absence of eye opening or verbal response, absence of brain stem reflexes, absence of motor response to noxious stimuli, details of apnea test \rightarrow time of test initiation, preapnea and post-apnea pH and PaCO₂, use of ancillary testing, indication, and interpreting physician's name, results of repeat neurological examinations, if performed, time and reason for contacting medical examiner, if appropriate.

Hypoxic-Ischemic Injury after Cardiac Arrest

- <10% survival for out-of-hospital cardiac arrest after CPR (*NEJM*. 2004;351:632).
- <20% survival to d/c for in-hospital cardiac arrest after CPR (*Resuscitation*. 2003;58:297).
- ↑ Duration of anoxia prior to CPR and ↑ duration CPR \rightarrow ↓ outcome (*Crit Care Med.* 1995;23:18)
- NOTE: prognostication, as detailed below, has been studied primarily in patients NOT treated with hypothermia

Prognosis After Cardiac Arrest (Neurol. 2006;67:203)

Neurological Examination: absence of pupillary and corneal responses has strong predictive value w/in 1–3 d post-arrest. Eye opening and spont eye mvmts may occur early w/o indicating good outcome; best predictive value after 3 d. Motor response is stronger predictor than overall GCS score and is most specific for poor outcome after 3 d. Single seizure and intermittent focal myoclonus do NOT predict poor outcome, but in patients not treated with hypothermia, diffuse myoclonus strongly a/w in-hospital death and poor outcome even if brainstem reflexes intact (*Neurology*. 2006;66:62).

Good outcome may occur rarely in patients with diffuse myoclonus who have been treated with hypothermia (*Neurol*. 2009;72:744).

MRI: absence of diffusion restriction on DWI/ADC a/w better neurologic outcome (*Mayo Clin Proc*. 2007;82:828). Common DWI/ADC abnormalities include cortical ribbon, watershed infarct, thalamus, basal ganglia.

EEG: generalized suppression \leq 20 μ V, burst suppression w/ generalized epileptiform activity, or generalized periodic complexes on isoelectric background strongly a/w poor outcome, but prognostic accuracy remains limited pending further studies.

Alpha coma pattern is NOT a/w poor outcome (Neurology. 1988;38:773).

SSEPs: more accurate prognostic tool than EEG b/c less confounding by medications and metabolic encephalopathy. B/l absence of N20 w/ median nerve stim strongly predicts poor outcome. Insufficient data for prognostic value of BAERs and VEPs.

Biochemical Markers: neuron-specific enolase (NSE) >33 mcg/l at day 1–3 a/w poor outcome. Serum astroglial S100 does not have prognostic value.

ICP and Brain Oxygen Monitoring: insufficient evidence for prognostic value.

	Waterallia and Change of	Deat Chance of	
Time After Arrest	Virtually no Chance of Regaining Independence	Best Chance of Regaining Independence	
Initial Exam	No pupillary light reflex	Pupillary light reflex present Decorticate or decerebrate posturing Conjugate roving or orient- ing eye mymts	
Day 1	Motor response no better than decorticate posturing Spontaneous eye mymts neither orienting nor roving conjugate	Motor response withdrawal or better Eye opening spontaneously or to noise	
Day 3	Motor response no better than decorticate posturing	Motor response withdrawal or better NL spontaneous eye mvmts	
1 Wk	Not following commands Spontaneous eye mymts neither orienting nor roving conjugate	Motor response obeying commands	
2 Wks	Abnormal oculocephalic response No improvement in eye opening	Normal oculocephalic response	

THERAPEUTIC HYPOTHERMIA FOR COMA AFTER CARDIAC ARREST

Mechanisms of Action: reduces cerebral metabolic rate and oxygen demand. Reduces cerebral edema and ICP by preserving blood brain barrier integrity. Reduces excitotoxic neuronal injury. Minimizes free radical release. Suppresses inflammation.

Supporting Data: study protocols vary, but mortality and neurological recovery benefits demonstrated by multiple randomized trials (NEJM. 2002;346:549; NEJM. 2002;346:557). Data exist only for out-of-hospital, VF/VT cardiac arrest; no data for PEA, asystolic arrest, or in-hospital arrest \rightarrow therapeutic cooling for these types of cardiac arrest may be applied at the discretion of the clinician (Circulation. 2003;108:118). Therapeutic cooling NOT proven to be beneficial for coma

after primary respiratory arrest w/o concomitant cardiac arrest. Hyperthermia is detrimental: odds ratio for unfavorable outcome is >2 for each 1°C increase in temp after arrest (*Arch Int Med.* 2001;161:2007).

Basic Principles and Approach to Therapeutic Hypothermia: initiate cooling rapidly. Multiple cooling methods may be required to meet temp goal 32–34°C (89–93°F).

Total cooling period 24 hrs, begins when cooling is initiated, NOT when target temp is reached. hivering generates heat and contributes to neuronal injury by increasing cerebral metabolism \rightarrow edation and paralysis may be necessary for duration of cooling.

Preparation for Hypothermia: laboratory evaluation: complete metabolic panel, CBC, PT/PTT, fibrinogen, d-dimer. Place arterial line for BP monitoring. Temp monitor for continuous assessment of core temp \rightarrow bladder temp probe, or pulmonary artery temp probe if oliguric (bladder temp probe requires presence of urine in bladder).

Inclusion Criteria: must be comatose w/in 6 hrs of cardiac arrest.

Relative Exclusion Criteria (hypothermia may carry \uparrow risk): Major head trauma \rightarrow rule out ICH by head CT prior to cooling if clinical suspicion for head trauma at time of arrest. Recent major surgery (w/in 14 d). Systemic infxn/sepsis \rightarrow hypothermia interferes w/ immune function. Other etiology for coma (i.e., drug/EtOH) pre-existing prior to arrest. Active bleeding \rightarrow hypothermia \downarrow clotting factor activity. Admin of thrombolytic, anti-platelet, or anticoagulation meds for cardiac condition is NOT a contraindication to hypothermia.

THERAPEUTIC HYPOTHERMIA PROTOCOL (MAY VARY BY INSTITUTION)

- 1. External Cooling w/ Cooling Blankets and Ice: obtain two cooling blankets and cables (one machine) to "sandwich" the pt → place sheets b/n blankets and pt to protect skin. Use additional cooling methods as needed to bring pt to goal temp. Pack ice in groin, sides of chest, axillae, and/or side of neck. Infuse cold saline via peripheral line or femoral venous catheter → 30 cc/kg of 4°C normal saline over 30 min. Do NOT infuse cold saline via jugular or subclavian catheter, as safety of cooling via these methods has not been studied. Avoid packing ice on top of chest → may impair ventilation. Paralyze w/ cisatracurium → 150 mcg/kg bolus then continuous infusion of 2 mcg/kg/min. Sedate w/ propofol → bolus (optional) 0.3–0.5 mg/kg followed by continuous infusion of 1 mg/kg/hr while pt is paralyzed or sedate w/ midazolam → bolus (optional) 0.05 mg/kg followed by continuous infusion of 0.125 mg/kg/hr. Once at goal temp can d/c ice bags, use cooling blankets to maintain.
- 2. External Cooling w/ Cooling Vest Devices: set target temp goal on device. Medicate for shivering w/ sedating and paralyzing agents. Consider secondary temp monitor → record pt temp on cooling vest device, secondary temp source and follow water temp of the cooling device → water temp indicates work device must perform to keep pt at target body temp.
- 3. Monitoring and Supportive Therapy During Hypothermia: monitor vitals closely. No indication for BIS or train-of-four monitoring during hypothermia; Consider EEG monitoring to diagnose subclinical status epilepticus masked by neuromuscular blockade (Neurorit Care. 2009;11:338). MAP > 90 mm Hg to maximize cerebral perfusion → potentially additive neuroprotective effects of high perfusion pressure w/ hypothermia. MAP goal lowered at discretion of clinician, depending on cardiac effects of high afterload or coronary vasoconstriction. If serious cardiac dysrhythmias, hemodynamic instability or bleeding during cooling, stop cooling process, and

actively re-warm pt. Osborn waves (positive deflection b/n QRS complex and ST segment) or bradycardia may develop during cooling \rightarrow no indication for specific therapy. Check blood cultures at 12 and 24 hrs after initiation of cooling \rightarrow hypothermia may mask infection. Check electrolytes, CBC, and glucose at 12 and 24 hrs \rightarrow hypothermia may cause hypokalemia, especially during concurrent insulin administration; rewarming may cause hyperkalemia due to K⁺ efflux from intracellular compartment. Hyperglycemia and increases in serum amylase and lipase may occur during cooling. Goal PaCO₂ 35–45 mm Hg \rightarrow analyze all ABGs at pt's body temp. Examine skin for burns q2 hrs if using cold blankets.

4. Rewarming: Basic Principles: Do NOT rewarm faster than 0.5°F per hour → passive or controlled rewarming should take 8–12 hrs. Shunting of cardiac output to re-opening peripheral vascular beds may cause hypotension. Monitor closely for hypotension, hyperkalemia. Aim for normothermia once rewarming phase is completed. Maintain paralytic and sedative therapy until temp of 36°C (96.8°F) is reached → first discontinue paralytic, then sedative once pt demonstrates motor activity or once train of 4 is achieved on monitor. rewarming After Cooling Blankets +/- Ice: remove cooling blankets (and ice if still in use)

Rewarming After Cooling Vest Use: program device for controlled rewarming over ~ 8 hr \rightarrow dial in the desired warming rate on the machine, then keep device in place and program for target temp of 37°C (98.6°F) for the next 48 hrs.

Decompressive Craniectomy

Indications: reverse mass effect and brain tissue shifts, decrease intracranial pressure, and improve cerebral perfusion pressure. Craniectomy lowers ICP by 15%, opening dura lowers ICP by 70%. Considered for: cerebral mass lesions, Intracerebral hemorrhage, subarachnoid hemorrhage, malignant cerebral edema from stroke, hemispheric encephalitis

Technique: removal of skull and incision of dural layer covering the brain for: upward expansion of swollen brain tissue through skull opening, rather than downward herniation which would compress brainstem; evacuation of brain hematoma; resection of mass lesion

Malignant Edema After MCA Infarct

- Epidemiology: 10% of strokes develop malignant cerebral edema (Stroke. 1985;16(2):282)
- Clinical Presentation: NIHSS score >15 for right, >20 for left hemispheric infarctions
- Forced gaze deviation, visual field cut, hemiplegia, aphasia or neglect. 78% mortality rate due to temporal lobe herniation w/ brainstem compression/torque (*Arch Neurol*. 1996;53:309)
- *Imaging Predictors:* head CT: large hypodensity >50% MCA territory most important predictor of malignant edema, herniation and death (*AJNR Am J Neuroradiol*. 1994;15:9); septum pellucidum midline shift >5 mm. Brain MRI: volume of infarct >80 cm³ on DWI (*Stroke*. 2003;34:1892). CTA/MRA: large vessel occlusions (ICA, proximal MCA)
- Clinical Predictors: age: <50 yrs. Early onset ↓ 'd consciousness. n/v <24 hr; SBP > 180 mm Hg <12 hr. Elevated white blood cell count. Heart failure (Stroke. 2001;32:2117)
- Evidence: RCTs: HAMLET, DESTINY, DECIMAL 93 pts, <55 yo Rx <48 hr for large MCA infarct w/ decompressive hemicrani. 1-yr favorable outcome (mRS 0-4): 75% craniectomy pts, 24% control group; mRS 3 or less: 43% craniectomy, 21% control group. 1-yr survival: 78% hemicraniectomy, 29% control group. Benefit offset if there was delay to surgery >3 d.

Edema After Cerebellar Infarcts

• *Neurological Emergency:* swelling can cause hydrocephalus due to compression of 4th ventricle, brain stem compression by upward transtentorial or tonsillar herniation

- Clinical Presentation: unsteady gait, n/v, HA, dizziness, diplopia, dysarthria, anisocoria.
- Rx: (1) Medical: mannitol, hypertonic saline, hyperventilation (for acute herniation syndromes); (2) Surgery: suboccipital craniectomy w/ possible resection of infarcted brain and ventriculostomy. Maintain ventriculostomy post-op until clear evidence of no sig hematoma or continued mass effect/edema. Suboccipital craniectomy: life-saving if medical Rx unable to prevent progression of swelling or clinical deterioration. Should be performed prior to clinical decompensation; do not wait for medical therapy to fail in a pt w/ a large stroke and clear progression of 4th ventricular compression; hydrocephalus can occur acutely, and lead to rapid, fatal deterioration. Considerations: time from symptom onset, size of infarct, pt's age, potential for neurological recovery. Most pts recover w/ relatively good quality of life.

Intracerebral Hemorrhage

- *Indications:* cerebellar hemorrhages >3 cm w/ clinical deterioration, brainstem compression, or hydrocephalus (*Stroke.* 2007;38:2001). Cerebral hematoma evacuation controversial: considered for supratentorial lobar clots w/in 1 cm of cortical surface. *Relative contraindications*: advanced age, serious medical co-morbidities, stable clinical condition, remote onset of hemorrhage, bleed in dominant hemisphere
- STICH trial: international Surgical Trial In Intracerebral Hemorrhage (Lancet. 2005;365:387)
- Patients with hematomas ≤1 cm from cortical surface more likely to have favorable outcome from early surgery (i.e., within 24 hr of randomization). However, the results are not statistically significant

Subdural Hematoma: bleeding b/n dura and arachnoid layers. *Prognosis:* mortality rate 40–60%. Outcomes based on age, GCS score. Negative impact: contusions, subarachnoid or intraventricular hemorrhage. *Head CT:* hematoma thickness, volume, midline shift, patency of basal cisterns. *Surgery:* craniectomy w/ better outcomes than burr hole evacuation (*Neurosurgery*. 2006;58:S2–16.). Rx w/in 2–4 hrs of neurological decline a/w lower mortality, 30% if early surgery vs. 80% if delayed. *Indications:* acute SDH and coma (GCS score <9) on arrival. Clot thickness >10 mm or midline shift >5 mm, regardless of GCS score. Decrease in GCS score by 2 or more points from time of trauma to presentation. Anisocoria or dilated/fixed pupils. ICP > 20 mm Hg

Epidural Hematoma: bleeding b/n dura and skull. *Prognosis:* 10% mortality. Head CT: hematoma volume, midline shift, brain swelling. *Indications for surgery:* hematoma volume >30 cm³, regardless of GCS score. Midline shift >10 mm. Acute hematoma, coma (GCS <9) w/ pupillary abnormalities. Early signs of herniation. Elevated intracranial pressure.

Postoperative Care: (1) Swallowing precautions, incentive spirometry, crystalloid fluids. (2) Prevention of intracranial pressure elevation. (3) Airway management: risk of airway collapse due to prolonged recovery of consciousness, especially in cases of brain retraction during surgery. (4) Refractory nausea, vomiting after posterior fossa surgery more common in women: ondansetron 1–4 mg IV or promethazine 12.5–25 mg IV. (5) Unrest, anxiety, discomfort due to endotracheal tube: dexmedetomidine, an alpha2-adrenergic agonist, ↓s anxiety w/o causing resp depression; approved for use only for first two postoperative days

Sample I	Postoperative Craniotomy Order	
Codeine 60 mg IM, q4h prn		
Cefazolin	500-1000 mg IV, q4h	
Dexamethasone 4 mg IV, q4h		
Phenytoin	100 mg, q8h (IV or PNGT)	
Subcutaneous heparin 5000 U, q8h		

Complications: meningitis, abscess, hemorrhage, stroke, cerebral edema, sz, air embolism

MECHANICAL VENTILATION IN NEUROLOGIC PATIENTS

- Mechanical ventilation for specific conditions
- Depressed level of consciousness: prevent aspiration, promote optimal gas exchange, start w/ controlled modes, and as drive recovers transition to assist modes
- *Elevated ICP*: for short duration (4–6 hr) can use hyperventilation to lower PaCO₂ to 30–35 mm Hg, ↓ 1–2 ml/min CBF/↓ 1 mm Hg PaCO₂; avoid worsening ICP elevation during intubation; avoid succinylcholine; propofol, lidocaine, or thiopental may lower ICP, but watch for hypotension; use etomidate if low BP; caution ischemia; rebound elevation in ICP if hyperventilating for extended duration.
- Central respiratory center lesions: controlled modes of ventilation initially to manage ↓ drive (e.g., Cheyne-Stokes respiration: bihemispheric lesions, metabolic encephalopathies; dorsolateral medulla: for example in Wallenberg syndrome can see hypo/apnea, Ondine's curse; pontine lesions: Cheyne-Stokes pattern, apneustic, ataxic pattern; pontomesencephalic junction injuries: hyperventilation; brainstem stroke: central or obstructive sleep apnea.
- Spinal cord injury: phrenic nerve paralysis, intercostals and abd weakness; caution with jaw lift, endotracheal intubation; may need tracheostomy in severe injuries; increased aspiration risk from ileus; watch for delayed apnea in high cervical injuries. Hypersensitivity to depolarizing blockade agents, seen esp. with denervating disease, extreme muscle disuse; avoid usage >48 hr, else severe hyperkalemia → cardiac arrest. Alternatives nondepolarizing agents.
- Neuromuscular ventilatory failure: (1) Acute polyneuropathy: autonomic instability $\rightarrow \downarrow$ BP with sedation (barbiturates, benzodiazepines, opioids), \uparrow K⁺ w/ succinylcholine (use non-depolarizing blockade); topical anesthetics (short acting benzodiazepines, atropine), blind nasal endotracheal intubation; SIMV and PS; bedside cardiac meds for resuscitation prn. (2) NMJ dz: exaggerated response to non-depolarizing agents, for example vecuronium; unpredictable response to succinylcholine. (3) Myopathies: AVOID succinylcholine; risk of hyperkalemia/rhabdomyolysis.

Recovery in neurogenic respiratory failure: ventilatory drive and chemosensitivity recover first \rightarrow wean from controlled to assist mode (SIMV or PS), can be hypercapneic at night when have decreased LOC, so controlled mode at night. Respiratory muscle strength recovery next \rightarrow PS mode, ensure adequate inspiratory pressure, or else RR.

NEUROVASCULAR CRITICAL CARE

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TRANSIENT ISCHEMIC ATTACKS

General: TIA: brief, reversible episode of focal neuro sxs (by definition <24 hr, most <1 hr). Newer definition: brief, reversible episode of focal neuro sxs due to ischemia w/ a negative MRI. Often hard to diagnose, given long differential. Longer TIAs more likely to be from an embolus, repeated TIAs w/ similar sxs suggest impending vessel occlusion. *Most TIAs should be worked up urgently*. Early w/u and treatment of TIA/minor stroke reduces risk of recurrent stroke by up to 80% (*Lancet Neurol.* 2007;370:1432)

Approach to Transient Neurologic Symptoms

Top 3: TIA, seizures (sz), migraines. *Others:* syncope, compressive neuropathy, anxiety, conversion, malingering, prior stroke sx re-manifested by metabolic derangement/infection, amyloid spells.

TIA: *Pts:* older, M>F, stroke risk factors (HTN, DM). *Sx:* negative (e.g., aphasia). If multiple modalities (i.e., sensory, motor) usu occur all at once. HA: sometimes. *Duration:* brief (usually ~15 min)

Seizures: pts: younger. Sx: Begins w/ positive (tingling) \rightarrow Negative (e.g., paresis, aphasia) postictally. *Duration*: very brief (secs-min). Negative can sometimes last hours.

Migraines: *pts:* younger, F>M, +FHx. Sx: HA after attack, N/V, photo-/phonophobia. Begins positive symptoms (sxs) (bright lights), followed by negative sxs. Slowly evolving (e.g., tingling spreads up arm). Modalities affected sequentially (e.g., vision \rightarrow sensory/motor) *Duration*: longer (30 min–hrs).

ISCHEMIC STROKES

Etiologies: *embolic:* sudden onset sxs, maximal at onset. Occasionally pt reports getting up to go to bathroom and developing symptoms. *Thrombotic:* full main deficit sometimes preceded by warning signs (either TIAs or minor symptoms) or stuttering course (progressive neurologic worsening over several hours).

Main Subtypes		
Large Artery Athero- sclerosis (~18%)	 Most common sites: carotid bifurcation, vertebrals at origin or at the vertebro-basilar junction, MCA at stem/bifurcation Rare for plaques to occur beyond first branching point Risk factors: HTN, DM, dyslipidemia, smoking 	
Cardio-Embolic (~21%)	 Afib, MI, CHF, prosthetic valves, rheumatic heart disease Most often lodge in MCA (especially superior division) or PCA territory Small embolus → cortical/penetrating arteries; large → main branches 	
Small Vessel (Lacune) (24%)	 Due to atherosclerosis → thrombosis of small penetrating vessels Infarcts up to 2 cm in size Often a/w HTN 	

Other Causes

- Vasculitis: Due to autoimmune disease, arteritis (temporal, Takayasu), infectious (Tb, syphilis, VZV), or primary CNS vasculitis
- **Dissections:** Strokes typically in younger pts (35–50 yo)
- **Fibromuscular Dysplasia:** Uncommon, affects women (30–50 yo). Imaging: string of beads (segmental narrowing and dilations of arteries), usu B/L. Arteries affected: renal, ICA > vert > intracranial a. Stenosis causes thrombosis or dissection. Rx: antiplatelet therapy
- Moyamoya: Best studied in Asians, but occurs worldwide. Occlusion of large arteries (usually distal ICA or main stem MCA/ACA) → lenticulostriate develops collaterals. *Angio*: collaterals = "puff of smoke" = moyamoya in Japanese. Stroke 2/2 large artery occl, ICH 2/2 breakdown/fragility of collaterals. *Rx*: surgical (↓ ischemic stroke): bypass (1st line) or EDAS (if bypass not feasible, involves laying branch of STA onto affected brain hoping it'll grow into brain)
- Drugs: Amphetamines and cocaine, cause either acute HTN or drug induced vasculopathy
- Subcortical Vascular Dementia: Elderly w/ longstanding HTN; Multiple subcortical infarctions → dementia. MR: extensive white matter changes. Rx: Alzheimer meds not found to be helpful (*Lancet Neurol.* 2008;7:310).
- Cadasil (Cerebral *a*utosomal *d*ominant *a*rteriopathy w/ subcortical *i*nfarcts and leukoencephalopathy): 30–50 yo, inherited (incomplete penetrance), Notch 3 mutation. P/w: lacunar strokes, progressive dementia, h/o migraine w/ aura. MR: extensive white matter Δ's. **Hypercoagulable States:** see below
- Unknown Causes: "Paradoxical embolism": technically "cryptogenic" (not lacunar, no clear cardioembolic (e.g., Afib)/large artery source. 2/2 PFO, see below for Rx.

Ischemic Stroke Work up

Urgent ED studies: CBC, BMP, PT, PTT, Cardiac Enzymes q8h × 3; Non-contrast head CT: r/o ICH (only required imaging for IV rtPA)

• Studies for secondary risk prevention:

Labs: Fasting lipid panel, including lipoprotein(a); Hemoglobin A1c (looking for underlying DM, glucose may be elevated s/p stroke); Homocysteine; TSH: looking for hyperthyroidism (increases risk of Afib); ESR and CRP if suspecting vasculitis or endocarditis; Hypercoagulable panel (before starting heparin): Antiphospholipid antibodies, lupus anticoagulant, Prothrombin G20210A Gene

Mutation, Factor V Leiden, Protein C/Protein S/Antithrombin III deficiencies, beta-2 microglobulin

Imaging: CTA: for endovascular intervention/medical therapy (e.g., dissection, atherosclerosis, vasculitis), comparable to U/S for ICA stenosis. MRI/MRA: not needed emergently, Se 95% w/in first few hours of stroke. Carotid U/S if CTA or MRA not done

Other tests: H/r: 24-hr Holter, looking for atrial fibrillation, in pts w/ high suspicion of afib can do extended cardiac monitoring for 7-14 d (or longer) as outpt. Echocardiogram: ruling out PFO or atrial septal aneurysm (in cryptogenic stroke), CHF, thrombus, left atrial dilatation (increases risk for afib), LV hypokinesis, valvular abn. Consider TEE for younger pts w/o clear cause, better for looking at valves. May be less sensitive for PFO detection than TTE if pt unable to Valsalva due to sedation. CT Venogram of lower extremities: for + PFO and cryptogenic stoke, to rule out DVTs; LE U/S do not evaluate for DVT in iliac veins

Thrombolysis: IV rt-PA in first 3 hr of sx onset (dose: 0.9 mg/kg, 10% as bolus): Can also be given

Early Management of Acute Ischemic Strokes

for select patients at 3-4.5 hr of sx onset (Stroke. 2009;40:2945). NNT for improvement: 3; number needed to harm: 30. Not used in minor/mild sxs, rapidly resolving symptoms, other contraindications (hemorrhage, AVM, endocarditis, abscess). Sooner $Rx \rightarrow$ better outcome (~2 million neurons lost every minute) (Stroke. 2006;37:263). BP prior to and during rt-PA: BP \leq 185/110 (If BP \uparrow , give Labetalol IV, if BP remains stable at target, then can give rt-PA). Post rt-PA precautions for 24 hr: No NG tube, NPO. No arterial sticks in non-compressible sites. No antiplatelets or anticoagulation (including DVT dosing of heparin and LMWH). Use TEDs/pneumoboots for DVT ppx. CT scan at 24 hr to determine if hemorrhage present, earlier w/ any clinical worsening. Hemorrhagic transformation: important complication of rt-PA: \uparrow risk w/ \uparrow NIHSS: score \geq 20 \rightarrow 17% risk, <10 \rightarrow 3% risk. Sxs: ↑ somnolence, HA, neurologic deterioration. If suspected: stop rt-PA, STAT noncontrast CT, coagulation panel, type and crossmatch 6-8 units platelets and cryoprecipitate. Negative CT: resume rt-PA (if still w/in 3 hr window); Positive CT: transfuse, neurosurgery consult. Angioedema (orolingual) in 5% receiving rt-PA, usu mild (Rx: steroids and anti-histamine)

Heparin: Guidelines do not recommend heparin; some centers consider it for large artery etiology (including actively embolizing carotid, some evidence) or for afib (little evidence); others: LV thrombus, mechanical heart valve, dissection, cerebral venous thrombosis. Do not give heparin if coma, large infarction, mass effect or ICH on CT, MAP > 130, NIHSS > 15.

Endovascular treatments: Chapter 19.

ASA: ASA 81 mg qd (full dose not proven more effective). No other antiplt tested acutely (e.g., clopidogrel, ticlopidine, dipyridamole). 2 large trials showed (nonsignificant) ↓ in death or disability w/ ASA w/in 48 hr (CAST and IST; Lancet. 1997;349:1641; Lancet. 1997;349:1569). Meta-analysis of both trials → modest/significant benefit: 7 strokes prevented/1000 pts treated, 4 deaths/1000; likely no effect on severity of current stroke but \(\psi \) recurrent ones.

Statins: For secondary prevention. Some rec high dose statin (as in ACS) acutely (for atherosclerotic stroke-see AHA/ASA guidelines 2008). A small study testing acute statin use, safety and efficacy trial, statin started <12 hr, not powered to detect clinical benefit, showed no difference in mortality/outcome. Recent statin withdrawal study (Neurology. 2009;69:904): Stopping outpt statin \rightarrow worse outcome (~5 \times \ \ \ \ in death/ dependence) and worse infarct volume; statin withdrawal may trigger pro-thrombotic/inflammatory response.

Induced HTN: Small clinical trials, useful in select group of pts, use w/ caution. Possibly \(\) BP restores perfusion to penumbra. How to do trial of HTN: consider in pts w/ fluctuating exam w/ BP changes (i.e., worse when \downarrow BP). Exclude pts w/h/o CAD, PVD, CHF, ischemic, ICH/midline shift, rt-PA, SBP > 200, heparin drip. \uparrow admission SBP by 20% (max SBP 200) w/ phenylephrine drip, titrate to neurologic improvement. If NIHSS \downarrow by 2 points after 30 min, continue drip. Daily attempt to titrate drip off, only if neurologic sx do not worsen during titration. Should be seen as bridge to more definitive therapy

General Medical Care

Hypertension: >60% of stroke pts have SBP > 160. Rx BP > 220/120, in pts *not* receiving t-PA, or if end-organ damage (kidney, heart, eye). Rx BP > 185/110 in pts receiving rt-PA. Don't \downarrow BP by >15%. Can initiate HTN meds w/in 24 hr of stroke.

Hypotension: worse outcomes, esp <100/70. Rx underlying cause of HoTN (volume depletion, arrhythmia, blood loss, sepsis). Rx: fluids, pressors

Glucose: *hypoglycemia*: goal BG 80–140, Rx w/ ISS or insulin drip. 1/3 stroke pts affected, a/w poor outcomes, few studies in stroke pts, studies extrapolated from other scenarios (Medical/Surgical ICU). *Hyperglycemia*: promptly correct hypoglycemia (may mimic strokes)

Temperature: fever: ↑ mortality, seek cause of fever and Rx w/ antipyretic. *Hypothermia*: ↓ mortality, insufficient data for use of cooling in stroke

Oxygenation: keep O_2 Sats $\ge 92\%$. Pts needing intubation have 50% mortality at 30 d. Aspiration PNA important complication and leading cause of death

Acute Stroke Treatment Evidence *Rt-PA*

NINDS rtPA (*NEJM.* 1995;333:1581): 624 pts, placebo vs. rt-PA w/in 3 hr, 2 parts: part 1: no diff in neuro improvement @ 24 hr vs. placebo. Part 2: favorable outcome vs. placebo @ 3 mos (OR for favorable outcome 1.7). ↑ benefit for pts treated w/in 90 min, no difference in mortality.

ECASS (*JAMA*. 1995;274:1017): European trial, multi center, 620 pts, placebo vs. rt-PA w/in 6 hr, sl. larger rt-PA dose. Overall no difference at 3 mos in rt-PA vs. placebo, ↑ mortality w/ rt-PA. Post hoc analysis: (nonsignificant) trend → better outcome w/ pts Rx'd w/in 3 hr

ECASS II (*Lancet.* 1998;352:1245): 800 pts, same dose as NINDS (0.9 mg/kg), w/in 6 hr. No benefit w/ rt-PA, not enough pt to see if Rx w/in 3 hr makes a difference.

ATLANTIS (*JAMA*. 1999;282:2019): Rt-PA 3–5 hr, 613 pts. No difference in functional outcome and mortality, Extending window >3 hr not beneficial

ECASS III (NEJM. 2008;359:1317): 821 pts, Rt-PA 3-4.5 hr. Rt-PA \rightarrow sl. better outcome @90 d.

Complications of ischemic stroke:

Ischemic brain swelling: see Chapter 19. Hemorrhagic transformation: \sim 5% of infractions \rightarrow symptomatic ICH, Rx: depends on extent. Sz's: risk \sim 2%, \uparrow w/ cortical strokes, no need for prophylactic AED, commonly partial sz (+/- secondary generalization)

Secondary Stroke Prevention Antiplatelets

ASA: High and low-dose equal efficacy. ↑ ASA dose doesn't ↓ stroke risk but ↑'s risk of bleeding Dipyridamole and ASA: French Toulouse Study/AICLA: no benefit of adding dipyridamole to ASA. ESPS-2 trial: ASA ↓ relative stroke risk by 18%, ASA/ext.-release dipyridamole by 37%; neither affected mortality (*J Neuro Sci.* 1996;143:1). HA most common SE of dipyridamole (↓ this by giving med qday w/ baby ASA × 1 wk then dropping ASA and switching med to BID)

Clopidogrel: Used if pt allergic to ASA, conflicting evidence. *CAPRIE*: (*Lancet*. 996;348:1329): Clopidogrel more effective than ASA in a *composite* risk of ischemic stroke, MI, or vascular death. But in pts w/ prior strokes, the benefit was *not* statistically significant, nor was stroke as an outcome reduced for the total population. *CHARISMA*: ASA vs. ASA + Clopidogrel in vascular pts and those w/ vascular risk factors, no difference in composite risk stroke, MI, or vascular death, but sig increase in bleeding events (*NEJM*. 2006;354:1706). *MATCH*: clopidogrel vs. ASA + clopidogrel in stroke pts, no difference for stroke or other endpoints, combination caused increased bleeding (*Lancet*. 2004;364:331). *PROFESS*: clopidogrel equivalent to combination ASA + Dipyridamole in >22,000 stroke pts (*Lancet*. 2008;7:875)

Extracranial Atherosclerosis

Carotid Endarterectomy (CEA): Indications: symptomatic stenosis: stenosis 70%–99% and life expectancy >5 yrs. 50%–69% stenosis: men w/ at least 5 yr life expectancy; Women \rightarrow no CEA, medically manage. Asymptomatic stenosis: medically stable men w/ stenosis 60%–99% w/ life expectancy of at least 5 yrs. Women \rightarrow no CEA, medically manage

Carotid Artery Stenting (CAS): Few trials, mixed results (neg results 2/2 lack of technical expertise), no evidence CAS better than CEA. CAS may be app. for surgical high risk pts. CAS $\rightarrow \uparrow$ risk periprocedural stroke (w/in 30 d); stroke risk after similar to CEA (*Lancet Neurol*. 2008;7:885). Current guidelines: CAS for high risk surgical pts w/ stenosis >70% and sx.

- Extracranial/Intracranial Bypass: Used in carotid occlusion: sup. temp. a. anastomosed to MCA. 1985 International EC/IC bypass: no benefit (*Stroke*. 1985;16:397). (Criticism: pts w/ completed infarctions included, no perfusion studies). COSS Trial showed EC/IC Bypass + medical therapy not superior to medical therapy alone (*JAMA*. 2011;306:1983).
- Complete Carotid Occlusion (CAO): (Neurology. 2000;54:878): asx CAO stroke risk: 0% at 2 yrs, 4.4% at 3 yrs (i.e., benign prognosis). *Sx CAO stroke risk*: 19% at 2 yrs, 21% at 3 yrs → reasonable to consider intervention.

Intracranial Atherosclerosis

Medical Rx: Antiplatelets or warfarin. ASA usually given, but if severe flow-limiting \rightarrow consider anticoag to \downarrow progression. ~10% strokes and TIAs 2/2 intracranial stenosis (50–99% stenotic).

• WASID Trial (NEJM. 2005;352:1305): ASA vs. warfarin for intracranial stenosis: no difference in outcome. Pts on warfarin: therapeutic 63.1% of the time (little better than real life PCP monitoring). When INR in range, rate of ischemic stroke reduced from 25/100 to 5/100

Angioplasty/Stenting: recently available option, untested for long-term outcome.

Cardioembolism

Atrial Fibrillation: 75,000 strokes/yr. Anticoagulate w/ warfarin INR (2–3) w/in 2 wks of stroke/TIA. Warfarin superior to ASA in pts w/ afib and recent stroke/TIA.

• *ACTIVE Trial* (*NEJM*. 2009;360:2066): ASA vs. ASA/Clopidogrel. Latter had ↓'d composite risk of stroke, MI, death from vascular event, embolism but ↑ risk of major bleeding (including ICH). Stroke risk: ASA 3.3% vs. ASA/Clopidogrel 2.4%. Major hemorrhage: ASA 1.3% vs. ASA/Clopidogrel 2%. Number needed to treat to avoid one stroke was 111 pts. Cost ↓ 202,464 to prevent a single stroke/yr (*NEJM*. 2009;361:13). All pts received ASA at dose of 75–100 mg/d, but only ASA 325 mg shown to ↓ risk of stroke in Afib (*Circulation*. 1991;84:527)

CHF: Causes stasis and increased risk for thromboembolism. Use of warfarin in CHF controversial,

warfarin sometimes used in pts w/ very low EF (<20%), most guidelines don't routinely recommend it unless pt has DVT/PE, mobile LV thrombus, or afib. Main trials (no RCT w/ conclusive evidence yet): WASH: no difference between ASA and Warfarin (AHJ. 2004;148:157). WATCH: no difference, ended early due to poor recruitment, underpowered (J Card Fail. 2004;10:101). WARCEF: ongoing study, but underpowered to detect stroke as primary endpoint. Combining WATCH and WARCEF might give statistical power. For pts w/ CHF and recent TIA/stroke either warfarin (goal INR 2–3) or antiplatelets

LV Thrombus: Warfarin (goal INR 2–3) for 3–12 mos if acute stroke/TIA, +ASA if CAD

Atrial Septal Abnormalities: *PFO*: fetal anomaly, allows communication b/n atria. *Atrial Septal Aneurysm (ASA)*: redundant tissue in the region of the fossa ovalis, acts as a nidus for thrombus formation. Association between cryptogenic strokes in pts \geq 55 yo and PFO +/- ASA in one study. In pts <55 yo, PFO + ASA > ASA > PFO significantly a/w stroke. One study showed association w/ PFO/cryptogenic strokes and older pts (*NEJM*. 2007;357:2262).

- Rx: 4 main modalities: antiplatelet, anticoag, surgical closure, percutaneous closure. PICSS found no difference between aspirin and warfarin (Circulation. 2002;105:2625) but was a very limited substudy; probably did not study the proper population
- *Guidelines:* atrial anomalies w/ ischemic stroke: antiplatelets (use warfarin if pt is high risk or has concomitant DVT or PE). PFO closure: considered in pts who fail medical therapy (i.e., get recurrent cryptogenic strokes).

Valvular Heart Dz: *Rheumatic Mitral Valve Dz:* Warfarin (INR 2–3) recommended. If pt has recurrent embolism despite adequate warfarin, add ASA. *Prosthetic heart valve:* modern mechanical valve and ischemic stroke/TIA: Warfarin (INR 2.5–3.5); consider adding ASA if pt has another stroke despite adequate warfarin treatment. Bioprosthetic heart valve w/ ischemic stroke, consider warfarin w/ INR goal 2–3. *All other valvular dz:* antiplatelet agents.

Hypercoagulable States

Possible association w/ ischemic stroke/cerebral venous thrombosis in pts <50 yo. Strongest association w/ antiphospholipid antibody syndrome. If testing abnl, repeat at f/u (as can be abnormal acutely). Most guidelines recommend testing in pts <50 yrs old w/ venous thrombosis, no recs for acute ischemic stroke. Rx: controversial, usu for venous thromboembolism: warfarin; for arterial thrombus (ischemic stroke) ASA vs. Warfarin (except for Antiphospholipid Ab syndrome \rightarrow warfarin)

Antiphospholipid Antibody Syndrome: Acquired, can be a/w autoimmune dz (e.g., lupus), symptoms are recurrent pregnancy loss/thrombotic events.

• Dx: Clinical event + 1 Lab abnl: (1) Antibodies against: cardiolipin and Beta 2 glycoprotein I, or (2) Lupus anticoagulant (misnomer, not a test just for lupus pts, not an anticoagulant!). If lab test abnormal, recheck in 12 wks. Rx: anticoagulation for life (INR 2–3)

Prothrombin G20210A Gene Mutation: ↑ prothrombin synth by liver.

Factor V Leiden: Factor V mutation → resistant to degradation (by activated protein C). Screen w/activated protein C resistance

Protein C, Protein S, or Antithrombin III deficiencies: Very uncommon. Dx difficult due to false +'s, esp acutely after stroke. All $3 \downarrow$ decr in acute thrombosis/surgery, or hepatic dysfn (i.e., \downarrow decr production), heparin decreases antithrombin, warfarin/OCPs decrease protein C/S.

DISSECTIONS

35–50 yo; ICA dissection 3x more common than Vert, extracranial > intracranial. Unlike atherosclerosis, dissections usu affect distal segments of extracranial arteries. *Carotid dissection*: 2–3 cm distal to bulb, irregular stenosis, doesn't usu extend intracranially (passes through tight foramina often preventing extension). *Vert dissection*: most often in freely moveable areas: at C1/C2 (as the artery wraps around the cervical vertebrae) and b/n origin and entrance into intervertebral foramina (can extend intracranially)

Etiologies: *Trauma*: almost any form of trauma can cause it, for example, MVA, vigorous coughing, and chiropractic manipulation (estimation of 1 stroke per 20,000 spinal manipulation). *Genetic:* Ehlers-Danlos syndrome, Marfan's syndrome, fibromuscular dysplasia, polycystic kidney disease, homocytinemia, alpha 1 antitrypsin. *Other*: Smoking, HTN, OCP's, possibliy infections (especially URI).

Clinical Features: *ICA dissection*: triad: neck/face/head pain. Partial Horner's in <50% (symp fibers run along ICA, ptosis/miosis but no anhidrosis – those fibers run along ECA). Cerebral/retinal ischemia. Lower CN palsy (especially XII and VI, which run near ICA) in ~12%. *Vert Dissection*: HA/pain back of neck, then post. circ. Ischemia (e.g., dizziness, dysarthria)

Dx: Imaging: "flame-like" appearance, tapered vessel, crescent shape around lumen. Doppler (See >90%): high resistance flow in distal artery. MRA w/ fat suppression, or CTA

Rx: Asx dissections: ASA. Intradural dissections: anticoag risks pseudoaneurysm formation, SAH. Sx Dissection (extradural): Warfarin INR 2–3 (w/ heparin/LMWH bridge) for 3–6 mos until stenosis improves (on imaging) then switch to antiplt. Beyond 6 mos if pt still w/ sxs, otherwise switch to ASA (no benefit for prolonged anticoag if no symptoms). F/U monitoring at 3 then 6 mos w/ Doppler U/S, MRA, or CTA. Surgery/Neuro-Intervention if pt w/ sxs despite adequate anticoag: angioplasty and stenting, vessel occlusion by embolization, vessel coiling or ligations, and bypass procedures.

Prognosis: worse for intracranial dissections (a/w more severe sxs and bleeds). 72–100% dissections recanalize. Recurrence rate: 1%/ yr (risks lasts up to a decade), higher in first month 2%. No evidence that ASA and anticoag prevents dissections.

INTRACEREBRAL HEMORRHAGE (ICH)

10-15% of first ever strokes are ICH (35% mortality at 30 d \rightarrow half occur in first 2 d). Only 20% of pts w/ ICH are expected to be functionally independent at 6 mos. Classically, sudden focal neuro deficit, that slowly progresses, +/- HA/Vomiting. Volume of ICH and GCS on admission best predictors of 30 d mortality (ICH score).

- **Etiologies:** *HTN:* deep hemorrhage. In basal ganglia, pons, cerebellum, or deep hemispheric white matter. *Other*: vascular malformation, anuerysm, trauma, coagulopathy, cocaine, vasculitis, neoplasm, sinus thrombosis, CAA.
- ICH Score: (1) GCS: 3-4=2 points, 5-12=1 point, 13-15=0 points. (2) ICH volume (ml): $\ge 30 = 1$, < 30 = 0. (3) IVH: Yes = 1, No = 0. (4) Age: $\ge 80 = 1$, < 80 = 0 (5) Infranterntorial: Yes = 1, No = 0. 30 d mortality: (5+,4,3,2,1,0) points. $\rightarrow (100,97,72,26,13,0)$ % mortality.

Volume Estimation: ICH Volume: measured $(ABC)/2 \rightarrow A = longest diameter, B = diameter perpendicular to A, C = <math>\uparrow$ of slices \times thickness of 10 mm slices (if 5 mm, divide C by 2).

Clinical features and dx of ICH: 50% basal ganglia, 33% hemisphere, 16% brainstem/ cerebellum. Peak deterioration/swelling on day 3–7, but delayed edema can occur. Autonomic instability can occur (\uparrow RR, \uparrow or \downarrow HR, \uparrow Glucose).

- **Neuroimaging:** *CT*: CTA r/o underlying vascular lesion. Subarachnoid blood = aneurysm. Temporal hemorrhage = trauma. Fluid–fluid levels in hematoma = coagulopathy (e.g., warfarin). Rescan for changes in exam and on Day 2.
- MRI: consider imaging to rule out underlying mass, if suspect amyloid angiopathy. Hyperacute bleed: center → iso to hypointense on T2; rim → hypointense T1. Subacute: hyper on T2/T1. Chronic: hypo on T2/T1.

Rx: *Blood pressure*: overaggressively decreasing BP may drop cerebral perfusion pressure. Unclear what BP goal should be (guidelines SBP < 180; in practice many rec SBP < 140) (Stroke. 2007;38:2001). BP meds to use: Labetalol, Nicardipine, Esmolol.

- *Seizures*: Occur early in 4.2% of pts and 8.1% w/in 30 d (Epilepsia. 2002;43:175). Lobar ICH significantly increased risk (especially if extends to cortical ribbon). Prophylactic Rx: unproven benefit, no proof that it effects mortality/morbidity, consider in large cortical ICH
- Glucose: elevated glucose a/w increased mortality; Goal 100–140
- *Temperature*: Fever worsens outcome, seek out sources, treat w/ acetaminophen. Persistent fever (>24 hr) a/w poor prognosis and ventricular extension
- *DVT/PE Prophylaxis*: at admit, intermittent pneumatic compressions. One study showed no increase risk for bleed on day 2 of ICH onset (w/ 5000 units of heparin TID); likely LMWH is just as safe. Pt's w/ DVT/PE, probably should get IVC filter.
- Surgery: supratentorial ICH: STICH trial → surgical clot evacuation no effect on mortality (one subgroup showed a trend to better outcome but not statistically significant: lobar clots w/in 1 cm of surface and GSC ≥ 9). Cerebellar hemorrhage (not included in STICH): >3 cm w/ deterioration or brain stem/4th ventricle compression fair better w/ surgery. Minimally invasive surgery (e.g., endoscopic aspiration): info limited, need more trials.
- *Warfarin*: Rate ICH on warfarin = 0.3-0.6%/yr. Risk doubles for every 0.5 above INR 4.5. Warfarin-related ICH Rx: Goal INR < 1.4 (PT/INR q4h \times 24 hr). Vit K 10mg IV (takes 6 hr to normalize INR) and FFP (10-20 ml/kg, $\sim 4-6$ U, risk of vol overload, give furosemide in CHF pts)
- *Restarting warfarin*: Risk of stroke in Afib 5% per year, in pts w/ previous stroke it increases to 12%. Survivors of prior lobar ICH should not be restarted on warfarin (even if high risk pt for thromboembolic stroke; *Stroke*. 2003;34:1710). One retrospective trial concluded that restarting warfarin had low risk of recurrence of ICH.
- Other Drug Induced Coagulopathies:
- *Heparin:* Rx: protamine → 1 mg per 100 units of Heparin over last 3 hrs; q1h PTT × 4 then Q4. If Heparin stopped 30–60 min ago give 0.5 to 0.75, if 60–120 min give 0.375 to 0.5 mg, if >120 min then give 0.25 to 0.375)
- *Enoxaparin:* Rx: protamine → 1 mg per 1 mg of enoxaparin; Recheck PTT in 2–4 hr, it still elevated consider giving an additional 0.5 mg of protamine
- *ASA/Clopidogrel*: No evidence for Plt transfusion, restart ASA ~1 wk after ICH, Rx: Transfuse plts if count <100,000.

SEIZURES

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DIFFERENTIAL DIAGNOSIS OF SEIZURES

DDx: TIA; transient global amnesia (TGA); panic attacks and other anxiety manifestations, migraine; narcolepsy/other sleep disorders; tremor, nonepileptic myoclonus, dystonia/other movement disorders; pseudo-seizures, malingering, breath-holding spells; stereotypies in cognitively impaired individuals.

Transient ischemic attack (TIA): Signs (si)/symptoms (sx) usually (-), but can be (+) (e.g., jerking, rigidity, hallucinations, visual illusions). *Limb shaking TIAs*: a/w preocclusive disease (dz) in ICA or MCA, usually orthostatic. *Todd's paralysis* (transient weakness after seizures (sz)) can mimic TIA/stroke.

Migraine aura (e.g., visual illusions/hallucinations, acute mental status (AMS) change w/ basilar migraine) can mimic complex partial seizure (CPS); aura onset usually more gradual and duration less. HA after CPS can mimic migraine.

Syncope: Including "convulsive syncope": see below.

PROVOKED SEIZURES: ETIOLOGIES

Etiology of Provoked Seizures Primary Neurologic Disorders Acute/subacute neurologic insult head trauma, Meningitis/encephalitis, Brain abscess, Stroke, SAH, HIV encephalopathy, Cerebral anoxia, Hypertensive encephalopathy/ PRES, Eclampsia, Neurosurgery Structural abnormalities: mass lesions, Vascular malformations

Systemic Disorders

Metabolic: hypoglycemia, hyperglycemia, Hyperosmolar state, Hyponatremia, Hypocalcemia, Hypomagnesemia, Uremia, Hepatic encephalopathy, Porphyria, Hyperthyroidism Drugs: overdose, withdrawal (EtOH, sedatives); others (see below) Sleep deprivation

Drugs That Commonly Cause Seizures or ↓ Seizure Threshold

- Anticholinesterases (organophosphates, physostigmine)
- Antidepressants (e.g., welbutrin)
- Analgesics (e.g., meperidine, Tramadol)
- Antibiotics (e.g., fluoroquinolones, TMP/ SMX)
- Antihistamines

Hyperthermia

High fever: in children

- · Antipsychotics (phenothiazenes, butyrophenones, clozapine)
- · Chemotherapy drugs (etoposide, ifosfamide, cisplatinum)
- Beta blockers (propranolol, oxprenolol)
- · Local anesthetics (bupivacaine, lidocaine, procaine, etidocaine)

- Cyclosporine, FK506
- Hypoglycemic medications
- Isoniazid
- · General anesthetics (e.g., enflurane)
- Methylxanthines (theophylline, aminophylline)
- Narcotics (fentanyl, meperidine, pentazocine, propoxyphene, tramadol)
- Penicillins (esp. w/ renal failure)
- · Phenylcyclidine (PCP), stimulants (amphetamines, cocaine, ephedrine, MDMA (ecstasy), phenylpropanolamine, terbutaline)

WORKUP OF FIRST SEIZURE

NOTE: for status epilepticus or impending status (seizures >5 min or multiple seizures w/o return to baseline) \rightarrow proceed to the status epilepticus algorithm.

CLINICAL EVAL: HPI: preceding illness/fever, trauma; aura, ictal and postictal phenomena (e.g., confusion, depression, aphasia, embarrassment, exhaustion, sleep, fear, HA, amnesia, nausea, pain, perceptual distortions, psychosis, thirst, weakness)

PMH/ROS: early history (prenatal, birth, perinatal), febrile seizures, milestones (motor, language), birthmarks/other congenital anomalies, myoclonic jerks, photosensitivity, prior seizures, FHx of seizures, stroke, head trauma, CNS infections, diurnal variation, relation to menses, triggers (e.g., emotion, exercise, loud music, flashing lights, television, fever, menses, sleep deprivation, coughing), injuries during sz, number of sz ED visits past yr, prior AEDs and why d/c'd, prior studies (EEG, CT, MRI, PET, SPECT). GEN EXAM: skin exam for neuroectodermal disorders (e.g., neurofibromatosis, tuberous sclerosis). NEURO EXAM: focal abnlities (suggestive of underlying cause)

TESTS: (1) Labs: chem7, LFTs, serum and urine tox screen, AED levels, UA, ESR, CRP, CXR, (2) Imaging: CT before LP if focal deficits, r/o space occupying lesion or acute hemorrhage. MRI preferable if non-emergency. (3) LP if: suspect meningitis/encephalitis; all HIV + pts; elderly; focal deficits. (4) MRI +/- gado (r/o structural causes, e.g., tumor, stroke, infection, AVM); (5) EEG w/in 24–48 hr, or emergently if persistent MS Δ .

ANTIEPILEPTIC DRUGS (AEDS)

AED T	rade Names and Abbreviations	
Generic Name	Trade Name	Abbreviation
F	rst Generation ("Old") AEDs	,
Phenytoin	Dilantin	PHT
Carbamazepine	Tegretol, Tegretol XR, Carbatrol	CBZ PRM
Primidone	Mysoline	
Valproic acid	Depakote, Depakote ER, Depakene	VPA
Phenobarbital	Luminal, Solfoton	PHB
Ethosuximide	Zarontin	ESX
Benzos: lorazepam, diazepam, midazolam, clonazepam, clorazepate	Klonopin, Tranxene	LZ, DZ, MZ, CZP CLZ
Sec	ond Generation ("New") AEDs	
Felbamate	Felbatol	FBM
Lamotrigine	Lamictal	LTG
Gabapentin	Neurontin	GBP
Topiramate	Topamax	TOP
Oxcarbazepine	Trileptal	OXC
Tiagabine	Gabitril	TGB
Levetiracetam	Keppra	LEV
Zonisamide	Zonegran	ZNS
Pregabalin	Lyrica	PGB
Lacosamide	Vimpat	LCS
Rufinamide	Banzel	RUF

Choice of AED in the ICU: General Principles Special Considerations When Choosing an AED

Seizure type: *Narrow spectrum* (focal or tonic-clonic seizures): CBZ, OXC, PHT, PHB, PRM, GBP, PGB, TGB. *Broad spectrum* (focal + generalized, including myoclonic and absence): LEV, VPA, TOP, ZNS, LTG (less effective for myoclonic), FBM.

Adding Medications: When adding extra AEDs consider interactions w/ other AEDs.

Some combinations to monitor closely b/c pharmacokinetic or pharmacodynamic interactions (there are many more): PHB + VPA, PHT + CBZ, CBZ + LTG, ?VPA + LTG (\uparrow SE and efficacy).

Other meds? Consider interactions w/ other non-AED medications.

Elderly? Lower threshold for side effects, esp. cognitive dysfn, tremor, gait problems. CrCl, hepatic clearance \downarrow after age 65; albumin levels \downarrow w/ age – need to \downarrow doses of protein-bound drugs; generally use lower doses titrated more slowly.

IV formulations (when rapid titration is necessary): available for: PHT, VPA, LEV, PHB, LCS.

Side Effects, Interactions, Comorbidities, and Monitoring

	norbid Conditions on AED Choice	
	Use Cautiously or Avoid	
Liver dz	VPA, PHT, PHB, CBZ, LTG, ZNS, FBM	
Renal impairment	LEV, GBP, PHB, PGB, TOP, ZNS	
h/o renal stones	ZNS, TOP	
Arrhythmias	CBZ, PHT	
Pancreatic dz	VPA, CBZ	
Hypothyroidism	CBZ,OXC, PHT	
Hyponatremia (or risk for)	CBZ, OXC,	
Osteopenia	PHT > CBZ, PHB	
Obesity	VPA, PGB (↑ 10-50 lb), ?CBZ, ?GBP (↑ 5-10 lb)	
Anorexia / malnourished	FBT, TOP, ZNS	
PCOS	VPA	
Taking OCPs	CBZ, OXC, PHT, PHB, TOP (at dose >200)	
Bleeding diathesis	VPA	
Blood dyscrasias	CBZ	
Peripheral edema	PGB	
h/o hypersensitivity rxns	AEDs w/ risk of rash (esp. PHT, CBZ, LTG)	
Absence sz's	CBZ, OXC, TGB	
Myoclonic sz's	GBP, LTG, OXC, CBZ, TGB, PGB,	
Generalized sz's	GBP, CBZ, OXC, (may exacerbate)	
Psychiatric d/o	LEV, PHB	
AEDs Tha	at May Help the Condition	
Mood instability	OXC,VPA, LTG, CBZ	
HA	TOP, VPA, CBZ in children	
Neuropathic pain	GBP, OXC, CBZ, TOP	
Obesity	TOP, ZNS	
PLMS	CZP, GBP, TOP, ZNS	
Tremor	CZP, PBT, PRI, ELV, TOP	
Insomnia	TGB	

Co	mmonly Used Antiepi	leptic Agents in ICU
Drug Class	Dose	Adverse Effects
Benzodiazepines Lorazepam Midazolam	0.1 mg/kg at 2 mg/min, upto 8 mg 0.2 mg/kg bolus, 0.75–10 mcg/kg/min infusion	Sedation, paradoxical excitation, hypotension, respiratory depression
Phenytoin	20 mg/kg iv bolus, then 5–7 mg/kg/d	Rapid infusion-hypotension, arrhythmias Nystagmus, diplopia, ataxia, sedation, lethargy Idiosyncratic: rash, fever, bone marrow suppression, hepatitis, Steven Johnson Syndrome
Fosphenytoin	20 mg Phenytoin equi- valent (PE)/kg iv bolus	Hypotension, bradycardia, phlebitis
Phenobarbital	20 mg/kg iv bolus	Sedation, nystagmus, ataxia, nausea, vomiting
Propofol	30-200 mcg/kg/min	Hypotension, bradycardia, hypertriglyceridemia
Levetiracetam	500-1,000 mg iv/ po q12h	Sedation, nausea, vomiting
Sodium valproate	1,000–2,500 mg/d iv/ po in 2–4 divided doses	Sedation, diplopia, nausea, vomiting, diarr- hea, hepatotoxicity, pancreatitis, rash
Lacosamide	100 mg/d, upto 200–400 mg/d po/iv	Dizziness, nausea, vomiting, diplopia, blurred vision, fatigue, ataxia

STATUS EPILEPTICUS

Status epilepticus (SE): over 30 min interval: continuous seizure (sz), or >1 sz w/o full return of consciousness/return to baseline b/n sz's. Can be: focal vs. gen, convulsive vs. nonconvulsize.

- "Prolonged seizure": >5 min: signifies failure of sz termination and risk of status epilepticus (SE).
- "Impending status": >10 min (treated as SE)
- Clusters of szs: considered transitional state toward SE.
- Generalized convulsive SE (G between CSE): convulsions are evident clinically. (Includes tonic-clonic SE (most common), tonic-SE, clonic-SE, myoclonic-SE).
- **Nonconvulsive SE (NCSE):** electrographic SE w/o clinically evident "convulsions" (but other signs are present, for example, altered consciousness).
- **Refractory SE (RSE):** Ongoing sz following 1st and 2nd line drug Rx.
- **Epidemiology:** *GCSE*: most common neurologic emergency. In USA 50–200 K/yr. \sim 1/3 known epilepsy, \sim 1/3 new epilepsy, \sim 1/3 acute neurologic disturbance (proportions vary by age). 15% of pts w/ epilepsy will have at least 1 episode of status. Most common precipitant: withdrawal of AEDs or noncompliance w/ AEDs. *NCSE*: accounts for 25%–50% of all SE. In comatose ICU pts incidence \sim 30%. Incidence in medical ICU: \sim 0.5%; in neuro ICU: \sim 10%.
- **Refractory SE:** ~30% of SE cases (varies greatly w/ cause: for example, more likely w/ encephalitis, GTCs; less w/ low AED levels, drug withdrawal).
- Etiology of SE: Main risk factor: prior SE (25%), but most SE occurs w/o prior sz. In 1st time SE,

cause in order of increasing frequency [but varies by age]: tumor, trauma, infection, unknown, metabolic, anoxia, etoh/drugs, medication change, stroke. Most common type: GCSE, from evolution of primary or secondarily generalized GTCs.

Pathophysiology: Disruption of nl sz-terminating mechanisms. Includes intxns b/n neuronal injury and systemic disturbances (cause and caused by SE): *neuronal injury*: excitotoxicity, ↑ met. demand, ↑ blood flow, ↑ edema/mass effect. *Systemic disturbances*: pulmonary edema, high output cardiac failure, contraction band necrosis, cardiac arrhythmias, aspiration PNA, fever, metabolic disturbances (glucose, K, Na, Phos, pH), hypoxia, ATN, rhabdomyolysis → ARF.

Prognosis: *GCSE*: M&M vary w/ age, etiology, duration. Mortality: children ~3%; adults ~20%. Highest mortality: anoxic injury; Lowest mortality: AED, EtOH, or benzo withdrawal. Mortality ↑ 20% for SE lasting >1–2 hr; no obvious reln at longer durations.

NCSE: Prognosis less well understood. M&M generally < than GCSE, though cause is critical.

	Features	Score
Level of consciousness	Alert, somnolent, or confused	0
	Stuporous or comatose	1
Sz type	Simple or complex partial	0
	Generalized	1
	NCSE + Coma	2
Age	<65	0
1000	>65	2
Previous seizures	Yes	0
	No	1
Total		0–6

DIAGNOSIS

GCSE: suspect after witnessed sz w/o arousal after 5 min, or if subsequent sz. Distinguish from "sz cluster" (pt awakes between sz's) – less urgent, but risk of \rightarrow SE. Motor activity may \downarrow after multiple sz's. Pseudoszs/non-epileptic sz's: sometimes hard to distinguish from GCSE. Clues favoring GCSE: hypoxemia, \uparrow CPK, acidosis; clues against GCSE: avoidance behavior.

NCSE: Clinical picture + EEG evidence of nonconvulsive seizures >30 min. If routine EEG unavailable, interim hairline EEG is useful (but less sensitive.) Routine continuous EEG in ICU pts and required duration is controversial. 95% noncomatose pts have first sz in 24 hr. In comatose pts who get seizures: 80% in 24 hr, ~95% in 48 hr (Clin Neurophysiol. 2007;118(8):1660). Specific interictal patterns predict ↑ risk of delayed NCSE, for example, PLEDs. Benzodiazepine trial is useful when dx in doubt about NCSE, but must have clinical + EEG improvement to be diagnostic.

Criteria for Nonconvulsive Seizure

EEG pattern = nonconvulsive seizure if:

Duration >10 s and satisfies at least 1 of 3 primary criteria.

Primary criteria

- Repetitive generalized or focal spikes, sharp-waves, spike-and-wave, or sharp-and-slow wave complexes at ≥3Hz.
- Same as above but frequency <3/s + satisfies the secondary criterion (below)
- 3. Sequential rhythmic, periodic, or quasi-periodic waves at ≥1Hz and unequivocal evolution in frequency (gradually ↑ or ↓ by at least 1Hz), 1/s, e.g., 2–3/s), morphology, or location (gradual spread into or out of a region involving at least two electrodes). Evolution in amplitude alone or in sharpness w/o other change in morphology is not enough to satisfy evolution in morphology.

Secondary criterion

- Significant improvement in clinical state or appearance of previously absent normal EEG patterns (such as posterior-dominant "alpha" rhythm) following admin of rapidly acting AED (see next table: benzodiazepine trial).
- *Resolution of the "epileptiform" discharges leaving diffuse slowing w/o clinical improvement and w/o appearance of previously absent normal EEG patterns would not satisfy the secondary criterion.

Benzodiazepine Trial for Diagnosis of NCSE (Clin Neurophys. 2007;118:1660-1670)

Monitoring: EEG, pulse ox, blood pressure, ECG, respiratory rate w/ dedicated nurse Benzodiazepine trial: Sequential doses of rapidly acting short-duration benzodiazepine, for example, midazolam at 1 mg/dose. Between doses, repeated clinical and EEG assessment. Trial is stopped after any of the following: (1) Persistent resolution of the EEG pattern (and exam repeated) (2) Definite clinical improvement (3) Respiratory depression, hypotension, or other adverse effect (4) Maximum allowed dose is reached (e.g., 0.2 mg/kg midazolam)

Test is (+) if: Resolution of ictal EEG pattern resolves and EITHER: improvement in the clinical state OR: appearance of previously absent nl EEG patterns (e.g., posterior-dominant "alpha" rhythm). Test is equivocal if: if EEG improves but pt does not.

Treatment of Adult Convulsive Status Epilepticus

Significant morbidity and mortality w/ delayed Rx. Best to use preestablished time-based algorithm. *Pediatric status epilepticus:* see separate protocol and considerations in next section.

NCSE: optimal mgt less well defined than for NCSE, b/c morbidity and mortality is generally less; risks/benefits of aggressive sz termination are similar. *General principles*: (1) Promptly establish high therapeutic AED doses. (2) Tailor to clinical course, esp. level of consciousness. (3) Avoid intubation and drug induced coma if possible. (4) Otherwise follow algorithm for GCSE.

GCSE: See below for in-hospital/ED protocol. If at home w/ seizure clusters, prolonged sz, impending status: Rectal diazepam gel (diastat) 0.2 mg/kg, OR Sublingual lorazepam 1 mg, OR Nasal midazolam 0.1–0.2 mg/kg; Call EMS.

^{*}from Chong & Hirsch, 2005, who modified the criteria of Young et al., 1996.

Treatme	nt Algorithm for ADULT Status Epilepticus (In Hospital Rx)
Time	Interventions/Actions
0–30 min	0 min: Initial rapid assessment: airway, breathing, circulation 1 min: VS 2 min: monitor: O ₂ saturation, EKG 2–10 min: IV access (at least 2 IVs), send labs: CBC, chem7, Ca, Mg, PO ₄ , LFTs, AED levels, tox screen, ABG 5–10 min: THIAMINE 100 mg IV then D50 50 ml IV bolus (after thiamine) Prepare to intubate in case necessary Consider Antibiotics and LP, esp. if febrile or not known epileptic 5–10 min: LORAZEPAM 0.1 mg/kg IV (<2 mg/min) 10–20 min: PHENYTOIN (50 mg/min) or FOS-PHT (150 mg/min): 20 mg/kg IV
	 Begin PHT FOS-PHT concurrently w/ lorazepam. Monitor EKG, check BP q2 min. Use separate IVs – ativan and PHT not compatible Send PHT level ~20 min after load. Treat fever w/ antipyretics, cooling
30–40 min	If seizures persist PHENYTOIN (50 mg/min) or FOS-PHT (150 mg/min): 10 mg/kg IV • Monitor EKG, check BP q1 min. • Send second PHT level 20 min after load May use VALPROIC ACID (DEPACOTE) 30 mg/kg IV (150 mg/min) or LEVETIRACETAM (KEPPRA) 50 mg/kg IV (100 mg/min) as alternatives when FOSPHENYTOIN or PHENYTOIN contraindicated*
30–60 min	If seizures persist 40 min: PHENOBARBITAL (75 mg/min) 20 mg/kg over 5–10 min 50 min: INTUBATE (if not already done) INITIATE EEG MONITORING
50–60 min	If seizures persist 50–60 min: MIDAZOLAM 0.2 mg/kg IV (loading dose) (Preferred if BP is unstable) • Titrate dose (0.1–0.4 mg/kg/hr) to stop EEG and clinical sz's • IVF or pressors to support BP if needed OR 50–60 min: PENTOBARBITAL, 5 mg/kg IV (loading dose) for burst suppression • Titrate (0.3–9 mg/kg/hr, avg = 4 mg/kg/hr) for burst suppression • IVF to support BP if needed; pressors only if IVF fails or contraindicated • Maintain at 0.5–5 mg/kg/h × hrs before taper, watch for recurrence
	OR 50–60 min: PROPOFOL, 1–2 mg/kg load, 2–10 mg/kg/hr maintenance drip to stop clinical and EEG sz's or maintain burst suppression on EEG. Head CT if not done previously / clinically indicated
3–24 hr	Correct underlying cause of SE Adjust AED doses to therapeutic effect (w/ continuous EEG guidance)
24–48 hr	Taper midazolam, pentobarbital, or propofol after above is complete, while maintaining high therapeutic levels of PHT (18–30 mg/l) and/or PHB (25–50 mg/l) and/or VPA (70–120 mg/l) to avoid recurrent sz's.

Adapted from MGH SE treatment protocol. *Epilepsia. 2009;50(3):415–21, Neurology. 2006 25;67(2):340.

WEAKNESS IN THE CRITICAL CARE SETTING

GALEN V. HENDERSON, MD

Assessment in the ICU

Assessment can be difficult; establish means of communication with patient. Utilize a range of minimal movements to facilitate communication (forehead winking, eye blinks, mouth movements and head or limb twitches). Consider communication aids, language barriers.

History Before the ICU

• Detailed history; if information cannot be obtained from the patient, information may be obtained from family/friends.

Helpful Examples of History Before the ICU

- If the prodrome includes breathlessness and orthopnea suggesting hypoventilation: rule out myasthenia gravis.
- If a preceding upper respiratory, diarrheal illness: rule out Guillain–Barré Syndrome (GBS).
- The rate and pattern of onset to guide diagnosis and prognosis: progressive limb and trunk weakness developing over days or weeks suggest a progressive neuromuscular disorder; history of fatigability suggests neuromuscular junction abnormality.
- Systemic abnormalities (abdominal pain): suggests porphyria or diabetes.
- Dietary factors such as tainted food may have precipitated botulism

History While in the ICU

- Take note of any history of hypoxic-ischemic brain damage, sepsis, systemic inflammatory response syndrome (SIRS), organ failure, metabolic, or endocrine abnormalities.
- Medications used in the ICU such as anesthesia, sedation, antibiotics, neuromuscular blocking agents, and steroids are important. In addition, events which may have occurred in the ICU include stroke or central pontine myelinolysis.
- A systemic illness may obscure a neurological cause for the primary presentation.
- Persistent weakness or failure to wean from the ventilator following a routine anesthetic may suggest either an intercurrent event that has occurred for example stroke or that a previously unsuspected neuromuscular condition has become symptomatic.
- In patients who fail to wean following cardiac surgery, impaired diaphragm function manifest as orthopnea or failure to wean when supine may suggest phrenic nerve damage, while focal sensor loss may indicate a border zone (MCA-PCA) stroke.

CLINICAL EXAMINATION

- If ophthalmoplegia and/or bilateral facial weakness: consider GBS.
- If there is associated ptosis, this may indicate myasthenia.
- Pupils poorly responsive/non responsive: consider Lambert–Eaton Syndrome.
- Bulbar function: tongue movement and pharyngeal reflex.
- Neck flexion and shoulder abduction: assess weakness of respiratory muscles, diaphragm.
- Fasciculation and weakness in the extremities: motor neuron disease; fatigable weakness:

neuromuscular junction abnormality.

• Weakness of the extremities with sensory loss suggests critical illness neuropathy if no sensory loss: concern for critical illness myopathy.

Breathing Pattern

- In central brainstem lesions interfering with the generation of the respiratory rhythm: no volitional respiratory movement; respiratory muscle weakness: partial ventilatory response which is inadequate to maintain ventilation without support.
- Selective involvement of the phrenic nerve or diaphragm weakness: prominent orthopnea and paradoxical movement of the diaphragm.

INVESTIGATIONS

Weakness is often multifactorial; suggested tests based on clinical suspicion:

- Hematology, electrolytes, thyroid function, creatine kinase
- Cerebral or spinal imaging may show stroke or demyelination
- EEG may be helpful in showing partial epilepsy or subclinical seizures
- Cerebrospinal fluid may show malignant infiltration or inflammatory process
- Neurophysiology study for GBS, myasthenia, other neuromuscular process

Considerations for Weakness in the Intensive Care Unit

Primary neurological diagnosis (stroke, cerebral hemorrhage, GBS, myasthenia gravis, myotonic dystrophy, etc.)

Progression or exacerbation of pre-existing neuromuscular disorder

Complications of treatment (prolonged neuromuscular blockade, critical illness myopathy)

Unrelated event (seizure, stroke)

Factors Associated with Weakness After Critical Illness

Sepsis, systemic inflammatory response syndrome (SIRS), drugs, multiple organ failure

Metabolic: hypermagnesemia, hypophosphatemia

Status epilepticus

Neuromuscular - critical illness polyneuropathy, critical illness myopathy

Primary CNS inflammation – acute disseminated encephalomyelitis, multiple sclerosis

Stroke or cerebral hemorrhage

Hypoxic - ischemic encephalopathy

Drugs	Affecting Neuromuscular Junction
Neuromuscular blocking agents (non-depolarizing)	pancuronium, vecuronium, cis-atracurium, rocuronium
Antibiotics	aminoglycosides, clindamycin, tetracycline, quinolones, polymyxin, erythromycin
Local anesthetics	lidocaine
Antiarrhythmics	quinidine, procainamide
Beta-blocking agents	propranolol, atenolol, acebutolol, bisoprolol, labetalol, metoprolol, oxprenolol, pindolol, sotalol, timolol
Immunosuppressants	cyclophosphamide, cyclosporin
Calcium channel blockers	verapamil, diltiazem
Diuretics	*
Corticosteroids	
Statins	
Antiretrovirals	zidovudine, lamivudine
Others	lithium carbonate, interferon alpha, phenytoin, dantrolene, d-penicillamine

Causes of Weakness in the ICU

- Disorders of cortex and brainstem
 - Epilepsy status epilepticus
 - Vascular stroke, hemorrhage, or cerebral hemorrhage
 - Infection
 - Metabolic
 - Hypoxic ischemic encephalopathy
 - White matter disease toxic encephalopathy, posterior reversible leukoencephalopathy
 - Autoimmune encephalitis Hashimoto's, paraneoplastic
- Disorders of the spinal cord
 - Trauma including surgery
 - Acute epidural compression due to neoplasm, infection, hematoma
 - Acute transverse myelitis
 - Cord infarction
- Anterior horn cell
 - Motor neuron disease
 - Poliomyelitis and post polio syndrome
 - Paraneoplastic syndrome
- Multiple radiculopathies
 - Leptomeningeal disease
 - AIDS polyradiculitis
- Acute polyneuropathy
 - Acute inflammatory demyelinating polyneuropathy
 - Acute motor and sensory axonal neuropathy
 - Acute motor axonal neuropathy
 - Phrenic neuropathies
 - Critical illness polyneuropathy
- Others toxic neuropathies, vasculitis, diphtheria, porphyria, HIV, etc.
- Chronic polyneuropathies

- Chronic inflammatory demyelinating polyneuropathy (CIDP)
- Diabetic polyneuropathy
- Neuromuscular transmission
 - Myasthenia gravis
 - Lambert–Eaton myasthenic syndrome
 - Congenital myasthenic syndrome
 - Neuromuscular blocking agents
 - Botulism, snake bites, fish toxins, organophosphates, hypermagnesemia, poisoning
- Myopathy
 - Congenital
 - Periodic paralysis
 - Acid maltase deficiency
 - Myotonic dystrophy
 - Duchenne muscular dystrophy
 - Mitochondrial
 - Acquired
 - Inflammatory myopathy
 - Polymyositis, dermatomyositis
 - Critical illness myopathy
 - Diffuse non-necrotizing cachetic myopathy
 - Acute necrotizing myopathy of ICU
 - Others HIV related, sarcoid, hypokalemia, hypophosphatemia
 - Corticosteroids, rhabdomyolysis

Neuropathies

Acute Inflammatory Demyelinating Polyneuropathy (AIDP)

- About 1/3 of GBS patients require admission to the ICU for observation or mechanical ventilation because of respiratory insufficiency, severe bulbar weakness, pulmonary aspiration, autonomic instability causing cardiac arrhythmias.
- Ventilatory failure is primarily caused by inspiratory muscle weakness plus weakness of the abdominal and accessory muscles of respiration. Retained airway secretions leading to pulmonary aspiration and atelectasis also contribute.

Miller Fisher Syndrome

- Ataxia, areflexia, and ophthalmoplegia are the classical features.
- Diplopia (1/3 patients), ataxia (1/5 patients).
- Facial weakness, bulbar impairments with dysphagia and dysarthria, facial and lip paresthesia, mild proximal limb weakness (1/3 patients).

Acute Motor and Sensory Axonal Neuropathy (AMSAN) and Acute Motor Neuropathy (AMAN)

- Axonal neuropathies may present with paralysis developing rapidly over hours leading to respiratory failure.
- There may be extensive total paralysis of all voluntary muscles of the body, including the cranial and ocular muscles.
- CSF protein is raised but there should be <10 WBC.

• In both, all peripheral nerves including cranial nerves, may be unresponsive to electrical stimulation, even when the stimuli are of high voltage and duration.

Acute Intermittent Porphyria

- Uncommon autosomal dominant disease characterized by recurrent episodes of abdominal pain, psychiatric disturbances, seizures, and motor axonal neuropathy with autonomic features.
- May mimic GBS causing bulbar and ventilatory failure.
- Precipitated by heavy alcohol consumption and numerous medications such as diazepam, theophylline, barbiturates.

Critical Illness Polyneuropathy

- Acute sensorimotor axonal neuropathy with develops in the setting of SIRS, septic encephalopathy and/or multi-organ failure.
- Increased risk with insulin deficiency, hyperglycemia, hypoalbuminemia with or without corticosteroids and neuromuscular blocking agents.
- Delayed weaning, severe distal flaccid wasting and weakness, areflexia, and sensory impairment.
- A pure motor neuropathy in association with neuromuscular blocking agents is a variant which has been reported.
- To compound the diagnostic problem, neuropathy, neuromuscular blockade, and myopathy may all coexist in the same patient.
- Axonal degeneration of both sensory and motor fibers without evidence of significant inflammation or primary demyelination. Muscle shows scattered atrophic fibers in acute denervation and grouped atrophy in chronic denervation.
- Critical illness polyneuropathy is a self-limited disease and the prognosis is influenced by the severity of the underlying condition which itself accounts for most of the mortality.
- Outcome related to severity of sepsis, extent and severity of the neuropathy, time in the ICU, presence of hyperglycemia or hypoalbuminemia.
- If neuropathy is mild/moderate, the recovery is relatively rapid and complete.

Neuromuscular Disorders

Depolarizing Neuromuscular Blocking Agents

- Physically resemble acetylcholine, bind to activate and block acetylcholine receptors.
 - Succinylcholine is a short acting (2–5 min) agent it produces intense neuromuscular relaxation by causing prolonged depolarization of the postsynaptic receptors at the NMJ. Its sole use is to facilitate tracheal intubation.
 - Should be avoided in neuromuscular disease as hyperkalemia may follow its use. It can precipitate malignant hyperthermia.

Non-depolarizing Neuromuscular Blocking Agents

- Bind reversibly to the postsynaptic acetylcholine receptors antagonizing acetylcholine, but do not activate the receptors.
- They produce longer lasting neuromuscular blockade and doses are cumulative, particularly if there is renal or hepatic failure.
- The effects are enhanced by hyperkalemia, hypophosphatemia, and hypermagnesemia.

Prolonged Neuromuscular Blockade

- Defined as recovery from NMJ blocking agents 50–100% longer than predicted by pharmacological parameters.
- Particularly associated with steroid-based NMJ blocking agents and occurs after either short- or

- long-term blockade with nondepolarizing agents.
- It may be associated with prolonged use or high doses of these drugs, metabolic acidosis, hepatic or renal insufficiency hypermagnesemia or in association with corticosteroid, aminoglycosides or other anesthetic agents.
- Weakness should not persist beyond 2 wk after stopping the blocking agents and typically lasts for only a few days.
- Prolonged blockade should be considered in any patient who remains weak hours after discontinuation of NMJ blocking agents.
- "Train of four" stimulation, in which 4 equal pulses are delivered over 2 sec, is used to assess recovery from acute block. Lack of response indicates prolonged neuromuscular blockade but formal repetitive nerve stimulation is required for confirmation.
- Neuromuscular disease may be unmasked in previously undiagnosed cases by medications commonly used intra-operatively and in the recovery room or ICU.
- Patients with myasthenia gravis or the Lambert–Eaton myasthenic syndrome may have prolonged weakness after the administration of even sub-therapeutic doses of these agents.

Myasthenia Gravis

- Patients present with respiratory failure due to a myasthenic crisis (usually precipitated by infection, surgery, or inadequate treatment)
- Others may develop respiratory failure during the course of their disease, sometimes caused by a therapeutic cholinergic crisis.
- Associated bulbar weakness predisposes to pulmonary aspiration and acute respiratory failure necessitating urgent tracheal intubation and ventilation.
- Repetitive simulation typically shows a decrement which is maximal after the 4th–5th stimuli and is more marked at 3 Hz simulation. There is a post activation repair of decrement immediately after exercise, and post activation exhaustion when retested after 3 min of rest.

Botulism

- Caused by toxins from *Clostridium botulinum* (gram pos anaerobe)
- Acts at presynaptic region of the NMJ causing failure of release of acetylcholine.
- The classical form occurs after ingestion of food that contains toxin but increasing numbers of patients are being seen as a consequence of using contaminated opiates or unclean needles to inject drugs of abuse into infected skin lesions.
- Cranial nerve deficits: blurred vision, diplopia, ptosis, dysarthria, dysphagia.
- The weakness often affects the arms before progressing to the legs.
- Autonomic symptoms include dry mouth, unreactive pupils, and ileus.
- The condition may be suspected by prominent and early ocular signs (dilated sluggishly reactive pupils and ophthalmoplegia) and dysphagia.
- Definitive diagnosis: detection of toxin in serum, stool, or food by bio-assay.
- Electrodiagnosis may not be straightforward because the findings depend on the timing of the examination and the severity of the disease.
 - Patients with relatively mild disease may have "normal" or low normal compound muscle action potentials amplitude, show no clear decrement at low rates of repetitive stimulation, but demonstrate an increment of >40% after exercise or after high rates of repetitive stimulation consistent with this being a presynaptic disorder of neuromuscular transmission.
 - This increment is usually not as marked as in the LEMS and in general only seen in clinically weak muscles. Unlike LEMS and myasthenia gravis, there is no post-activation exhaustion and

the increment usually persists for 4–20 min. In more severe disease, the resting CMAP is usually small, there may or may not be decrement at low rates of repetitive stimulation, and the incremental response to high rates to stimulation may be minimal or absent.

Other Neuromuscular Transmission Disorders

• Organophosphate poisoning, tick paralysis, black widow spider, and certain types of snake envenomation.

Muscle Disease

Diffuse Non-Necrotizing Cachectic Myopathy

- Common and presents as muscle wasting with associated weakness.
- The CK levels and EMG are normal or show only mild changes.
- It is associated with prolonged ICU admission, sedation or paralysis causing muscle disuse, and poor nutrition and with protein catabolism during critical illness.
- There is proximal or general weakness. Biopsy shows type 2 fiber and neurogenic atrophy.

Critical Illness Myopathy

- Distinct form of myopathy which occurs in patient with critical illness on the ICU.
- There are many other names which include: myopathy with selective loss of thick filaments, acute quadriplegic myopathy, acute illness, acute myopathy of intensive care, rapidly evolving myopathy with myosin-deficient fibers.
- It is probably considerably more frequent than critical illness polyneuropathy.
- Associated with prolonged exposure to high doses of corticosteroids and nondepolarizing muscle blocking agents used to treat acute pulmonary disorders such as asthma.
 - It can occur in other situations including SIRS, a major organ transplantation, particularly liver, and it dies not seem to correlate with the duration of intensive care.
 - Other factors that may contribute include nutritional deficiencies, concurrent drug administration with aminoglycosides or cyclosporin, hyperglycemic, renal and hepatic dysfunction, fever, severe metabolic and electrolyte disorders.
 - The limb weakness is predominately proximal but may be generalized.
 - There may be facial and neck weakness as well, but the ocular movements are often spared, reflexes are reduced and sensation is not affected.
 - Blood CK levels are raised in <50% and electrodiagnostic studies are neither sensitive nor specific for diagnosing myopathy in the critically ill.
 - Better outcomes than after critical illness polyneuropathy, usually full recovery unless there has been severe and prolonged paralysis.

Acute Necrotizing Myopathy of Intensive Care

- Rare condition which may be a form on rhabdomyolysis.
- Develops after exposure to neuromuscular blocking agents with or without steroid therapy, but may be associated with other infective or metabolic insults.
- Serum CK is markedly elevated, there is usually associated myoglobinuremia
- EMG confirms severe myopathy and biopsy shows patch or widespread necrosis with occasionally vasculitis or infarction within the muscle.
- Prognosis for recovery of weakness is poor.

Other Myopathies

- Steroid myopathy (for example in asthma or COPD patients)
 - This is a slowly evolving, mild-to-moderate proximal weakness with mild elevation of CK and

- type 2 fiber atrophy.
- Sepsis may affect the muscles causing polymyositis due to septic micrometastases.
- Inflammatory myopathies cause respiratory weakness wind patient with dermatomyositis may have a characteristic skin rash.
- Muscular dystrophy may present with ventilatory failure.
- Myotonic dystrophy is occasionally identified for the first time in the ICU.
- In adults, acid maltase deficiency may present with proximal weakness, scoliosis and diaphragmatic paralysis.
- Rhabdomyolysis may be precipitated by trauma, compartment syndrome, ischemic arterial occlusion or drugs and is associated with high serum CK levels, myoglobinuria and general weakness.

Other Conditions

Tetanus

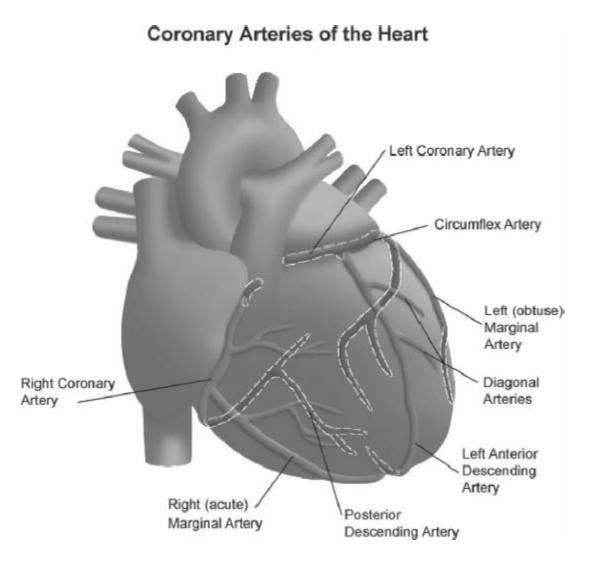
- Caused by tetanospasmin, a toxin in contaminated wound by the gram positive spore forming bacilli Clostridium tetani in unimmunized individuals.
- Toxin is transported in the spinal cord or brainstem or both.
- Migrates to the presynaptic terminals and inhibit the release of gamma-aminobutyric acid (GABA) and glycine, important inhibitory neurotransmitters.
- Most patients experience increased muscle tone and spasms.
- Respiratory compromise is caused by spasm of respiratory muscles or laryngospasm.
- Autonomic dysfunction in severe cases: heart rate and blood pressure lability, arrhythmias, fever, profuse sweating, peripheral vasoconstriction, ileus.
- Muscle rupture and rhabdomyolysis can complicate extreme cases.

Paralytic Rabies

- Produces neuromuscular weakness that can be difficult to differentiate from other causes of weakness such as GBS.
- May begin with local wound pain and paresthesias followed by fasciculations near the site of inoculation.

ACUTE CORONARY SYNDROMES AND MYOCARDIAL ISCHEMIA

NEIL J. WIMMER, MD • PETER H. STONE, MD



Chest Pain

Differential Dx (cardiovascular causes, pulmonary causes, GI causes, musculoskeletal causes, other)

- Cardiovascular causes: acute coronary syndrome (ACS) (unstable angina, MI), pericarditis, dissection, HTN emergency, aortic dissection, ruptured aortic aneurysm
- Pulmonary causes: pneumonia, pleuritis, PTX, PE, pulmonary HTN
- GI causes: GERD, esophageal spasm, Mallory-Weiss, PUD, pancreatitis
- Musculoskeletal/other causes: costochondritis, herpes zoster, anxiety/panic attack.

HTN Emergencies: Elevated BP (SBP > 180 or DBP > 120 mm Hg) causing clinical manifestations/end-organ damage

HTN urgency: Elevated BP that (by definition) is asymptomatic

• Etiologies: essential HTN, medication non-adherence, stroke, drugs (cocaine, amphetamines, renovascular disease, endocrine (pheochromocytoma), vasculitis, eclampsia/preeclampsia

- Work-up: history of HTN, med compliance, illicits/OTC use. ROS for HA, visual changes, chest pain, SOB, orthopnea, PND. Exam: bilateral BPs, JVP, rales, s3/s4, renal or flank bruits, peripheral pulses, funduscopic exam, mental status and neuro exam.
- Studies: electrolytes, renal function, UA, ECG, CXR, cardiac biomarkers. Possibly renal U/S, metanephrines, renin/aldosterone.
- Management: requires ICU admission. Decrease MAP < 20–25% in 1st min to 1 hr. Then decrease BP down approx 10% every 2–4 hrs until at goal. Initially avoid rapid drops in BP to allow for end-organ auto-regulation. Monitor UOP, renal function, mental status.

Possible therapeutic agents: IV labetalol, nicardipine, nitroprusside (be careful in renal/liver dysfunction), esmolol, hydralazine, enalaprilat.

Acute Coronary Syndromes

- Typical angina is defined as substernal pain, exertional angina is relieved by rest (NEJM. 1979;300:1350).
- Exam (key findings): check bilateral blood pressures to assess for aortic dissection. Pulmonary edema. New S4; new MR; exclude reproduction of pain from palpation; HF (S3, Kussmaul sign); femoral and carotid bruits (to assess for PAD)
- Electrocardiography: critical to obtain serial tracings.
 - Diagnosis of ischemia or infarction requires EKG changes in 2+ contiguous leads. (J Electorcardiol. 2010;43:91).
 - Localization of the infarct: Anterior (V1–V4); Apical/lateral (V5,V6); Inferior (II, III, aVF), III > II suggest RCA as culprit compared to LCx; Lateral (I, aVL); Posterior (inverse of V1–V3). (NEJM. 2003;348:933).
 - Differential Dx of ST elevation: MI, LVH, LBBB, LV aneurysm, Myopericarditis, early repolarization, hyperkalemia, Brugada pattern, Takatsubo cardiomyopathy (NEJM. 2003;349:2128).

Cardiac Biomarkers (Card Rev. 2010;18:12)

- Cardiac troponins are more sensitive than CK-MB.
- CK–MB useful for assessing infarct size and re-infarction.
- Differential Dx of elevated troponin that is not ACS: recent MI; CKD/ESRD (chronic troponin elevations are common (AJKD. 2007;49:507); CHF decompensation or volume overload; CMP (infiltrative or dilated); trauma (cardioversion/ICD shocks), chest compressions, SAH, PE, pulmonary edema, myopericarditis, shock.

Characteristics of Cardiac Biomarkers			
Serum Marker	Initial Increase	Time to Peak	Return to Normal
CK-MB	3–12 hr	24 hr	48–72 hr
Troponin T	3–12 hr	12 -4 8 hr	5-14 d
Troponin I	3–12 hr	24 hr	5-10 d

(NEJM. 1997;337:1648)

UNSTABLE ANGINA (UA) vs. Non-ST ELEVATION MI (NSTEMI)

ACS represents acute mismatch of myocardial oxygen supply and demand, spanning presentations of unstable angina \rightarrow NSTEMI \rightarrow STEMI.

Definition:

UA: acute myocardial ischemia without evidence of myocardial necrosis (biomarker negative). Angina that is new-onset, crescendo, or at rest. There may or may not be ECG changes, and by definition is cardiac biomarker negative. It is a clinical diagnosis.

NSTEMI: acute myocardial ischemia with evidence of myocardial necrosis (+ cardiac biomarkers).

Early Ri	isk Stratification: Multiple Risk Scores Available (TIMI, GRACE, PURSUIT)
TIMI R	Risk Score for UA/NSTEMI (1 point per factor)
Age >6!	5 yrs
3 or mo	ore risk factors for CAD (HTN, HL, DM, current smoking, FHx of CAD)
Prior co	pronary stenosis of 50%
ASA us	e in last 7 d
2 or mo	ore angina episodes in last 24 hrs
ST segn	nent deviation of >0.5 mm
Elevated	d cardiac biomarkers (troponin or CK-MB)

(JAMA 2000;284:835)

TIMI Risk Score Interpretation			
Score Rate of Death/MI/Revascularization in 14 d		14 d	
0-1	5%		
2	8%		
3	13%		
4	20%		
5	26%		
6-7	41%		

(JAMA. 2000;284:835)

TIMI risk score of 3 or more represents a higher risk group who benefit from "early invasive therapy" including cardiac catheterization within 24 hrs from onset of pain (JACC. 2003;41:81S).

Figure 1. Approach to UA/NSTEMI

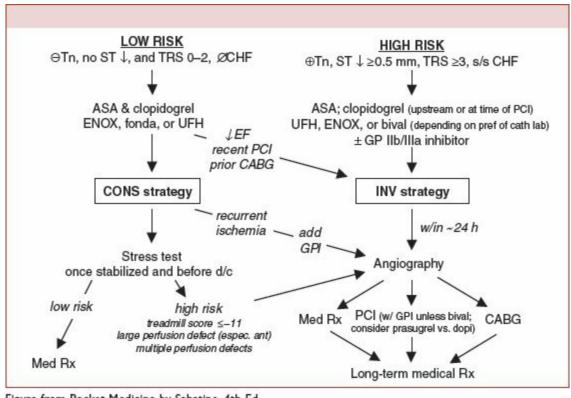


Figure from Pocket Medicine by Sabatine, 4th Ed.

Therapeutics

Anti-Ischemics: Nitrates, β-Blockers, Calcium Channel Blockers, Morphine, Oxygen

Anti-Ischemics: Nitrates,β-Blockers, Calcium Channel Blockers, Morphine, Oxygen		
Agent	Comment	
Nitrates, IV 20–200 mcg/min gtt, SL 0.4 mg q5min \times 3, topical 1–2 in. paste)	Decreases symptoms, no mortality change	
β-blockers e.g., metoprolol 5 mg IV q5min $×$ 3, then 25–50 mg PO q6h titrated to HR 50–60 bpm.	Decrease progression to MI (JAMA. 1988;260:2259). Contraindicated if HR < 60, SBP < 100, CHF, heart block, severe bronchospasm	
Calcium channel blockers (non-dihydropyri- dines alone, or dihydropyridines if adminis- tered with beta-blockers)	Only if patients cannot tolerate β -blockers.	
Morphine 1–2 mg IV doses until pain relieved.	If persistent pain.	
Oxygen	Titrate to keep SaO ₂ > 90%	
Statins	Survival benefit with high dose statin (atorvastatin 80 mg PO daily) (NEJM. 2004;350:1495).	

Antithro	ombotics
Agent	Comment
Unfractionated heparin 60 units/kg IV bolus (up to 4,000 units), then IV gtt at 12 units/kg (up to 1,000 units/hr)	Decrease death/MI approx 24% (JAMA. 1996;276:811).
LMWH For instance, enoxaparin 1 mg/kg SC BID × 2–3 d (daily if CrCl < 30)	Decrease approx 10% death/MI compared to UFH (JAMA. 2004;292:89).
Bivalirudin 0.75 mg/kg IVB at time of PCI then 1.75 mg/ kg/hr gtt	With PCI, bival alone similar outcomes to heparin and GP IIb/IIIa inhibitor combined with less bleeding (NEJM. 2006;354:1464).

Ant	tiplatelets
Agent	Comment
Aspirin $162-325 \text{ mg PO} \times 1$, then $75-325 \text{ mg daily}$	50%-70% decrease in death or MI (NEJM. 1988;319:1105).
Clopidogrel 300 mg-600 mg × 1, then 75 mg/d. Requires 6 hr to reach steady state	In addition to ASA, approx 20% decrease in death/MI/stroke (NEJM. 2001;345:494.)
Prasugrel 60 mg \times 1, then 10 mg/d	Approx 20% decrease in death/MI stroke compared to clopidogrel, but more bleeding. Avoid if >75 yrs, hx CVA. (NEJM. 2007;359:2001).
Ticagralor 180 mg \times 1, then 90 mg BID	More rapid and potent than clopidogrel. Approx 15% decrease in death/MI/stroke compared to clopidogrel, but increased bleeding (NEJM. 2009;361:1045).
GP Ilb/Illa inhibitors abciximab, eptifibitide, or tirofiban. Infusions given up to 24 hrs post PCI.	Can be given in addition to other antiplatelets. No clear benefit starting prior to PCI, but increase bleeding risk (NEJM. 2009;360:2176).

${\bf Angiography/Reperfusion\ The rapy}$

- Conservative Approach: medical therapy with predischarge stress test; angiography only if recurrent ischemia or positive submaximal ETT or markedly positive full-level ETT.
- Early Invasive Approach: angiography within 24–48 hrs
 - Approximately 25% reduction in death/MI (NEJM. 2001;344:1879).
 - Indicated if high risk: recurrent ischemia, positive biomarkers, ST segment deviation, TIMI score 3 or more, recent PCI, low EF.

ST-ELEVATION MI (STEMI)

- Diagnosis: more than 1 mm ST segment elevation in 2 contiguous leads (or new LBBB) in setting of angina.
- Reperfusion: maximal benefit derived when reperfusion is performed as early as possible. If available, PCI should be performed within 90 min of presentation.
- PCI strategy: Approx 25% less death, 65% less reMI, 50% less strokes, and 95% less ICH compared with reperfusion with lytics (Lancet. 2003;361:13).
- Transfer to PCI center is better if can be done in timely fashion.
- Lytic strategy (If primary PCI not available)
 - Approx 20% mortality decrease in AMI and approx 10% mortality benefit in IMI compared to no reperfusion if done in <12 hrs.
 - Increased risk of ICH in elderly.
 - Absolute contraindications: prior ICH, intracranial neoplasm/aneurysm/AVM, stroke or head trauma within 3 mo, active bleeding or known bleeding diathesis, suspected aortic dissection.
 - Relative contraindications: hx severe HTN, ischemic stroke >3 mo prior, prolonged CPR (>10 mins), trauma or major surgery in 3 wk, recent bleed or active PUD, noncompressible vascular punctures, pregnancy, current anticoagulation.

Adjunctive Therapies

	Antiplatelet Agents			
Aspirin Approx 20% decrease in death (Lancet. 1998;ii:349).				
Clopidogrel	lopidogrel No RCT of clopidogrel + ASA in STEMI			
GP IIb/IIIa	Pre-PCI approx 60% decrease in death/MI/revasc (NEJM. 2001;344:1895). No role with lytics			

Anticoagulants

Unfractionated Heparin: No clear mortality benefit in PCI, but used routinely. Increased vessel patency when used with fibrin-specific lytics.

LMWH: Can be used during PCI instead of UFH.

Bivalirudin: Decreased death and bleeding, but may cause more stent thrombosis compared to heparin and GP IIb/IIIa inhibitors (NEJM. 2008;358:2218).

Other Medications Used to Treat STEMI

• β-blockers: approx 20% decrease arrhythmic death or re-infarction, but increased risk of precipitating hypotension. (Lancet. 2005;366:1622). Contraindicated if HR < 60, SBP 100, mod-severe

CHF, high grade heart block, severe bronchospasm.

- ACE-inhibitors: approx 10% mortality benefit seen with anterior MI, if pulmonary edema, or EF < 40% (Lancet. 1994;343:1115).
- Angiotensin receptor blockers (ARBs): similar to ACE-I efficacy (NEJM. 2003;349:20).
- Other adjunctive meds: similar to NSTEMI with nitrates, statins, oxygen, morphine as above.

Intra-Aortic Balloon Pump

- Best anti-ischemic device
- Deflates in systole, reducing aortic volume, and creates a vacuum effect thereby reducing afterload
- Inflates during diastole improving coronary perfusion

Indications: cardiogenic shock, mechanical complications of MI (VSD, pap muscle rupture), refractory ischemia or VT/VF, facilitation of revascularization, critical valvular disease as a bridge to surgery.

- Contraindications: severe aortic insufficiency, aortic pathology (dissection, aneurysm, intramural hematoma), severe PAD, uncontrolled bleeding.
- Complications: vascular trauma/leg ischemia, platelet destruction and hemolysis, bleeding, infection, renal injury if mal-positioned.

INFECTION MYOCARDIAL INFARCTION (IMI) AND ITS COMPLICATIONS (Circ. 1990;81:401; Annals. 1995;123:509)

- Heart block (~20%). Rx with atropine, epi, isoproterenol, temporary pacing.
- RV infarct associated with hypotension, elevated JVP, Kussmaul sign. Rx with optimization of preload with goal RA pressure 10–14 (usually requires IVF) (BHJ. 1990;63:98); maintain AV synchrony (NEJM. 1998;338:933); pulmonary vasodilators (e.g., NO).

Mechanical Complications (Crit Care Med. 2007;35:S348)

- Account for ~15% of mortality after STEMI.
- Risk factors: age, female gender, Q waves, increased troponin levels
- When concerned: obtain STAT echo, repeat angiography +/- PA catheter insertion (with O₂ saturation run looking for shunt). May need urgent surgical evaluation.

Characteristics of IMI				
Early Complication	Clinical Features	Treatment		
Cardiogenic shock	Immediate post-MI. Hypotension, elevated JVP, elevated PCWP	PA catheters, inotropes, pressors, IABP, revascularization.		
Free wall rupture (or pseudoaneurysm)	2-3 d post-MI. sudden hypoten- sion to tamponade to PEA arrest	Volume resuscitation, inotro- pes, surgery, pericardiocentesis		
VSD	<5 d post-MI. new murmur	Inotropes, IABP, vasodilators, surgery		
Papillary muscle rup- ture (acute sever MR)	<5 d post-MI; new MR murmur	Vasodilators, IABP, surgery		

Late Complications

• LV aneurysm: occurs days to weeks post-MI. Risk factors: large/anterior MI, steroids, NSAIDS.

Apical dyskinesis/aneurysm increases risk of LV thrombus. Can compromise pump function or cause arrhythmia.

- LV thrombus: 10%–40% anterior MI. Increased embolization risk. Rx with anticoagulation 3–6 mo.
- Pericarditis: 2–4 d post MI. Pericardial rub/effusion, pleuritic CP, EKG changes. Rx with ASA (up to 650 mg q4h) > colchicine > Tylenol > steroids > other NSAIDs.
- Dressler's syndrome: late autoimmune carditis, more rare in reperfusion era. Similar rx to acute pericarditis.

Electrical Complications

- Atrial fibrillation: (10%–15%).
- VT/VF: early monomorphic VT does not have significant prognostic value. Treat with lidocaine/amiodarone/b-blockers.
- Bradyarrhythmias: range from sinus bradycardia to complete heart block. May require emergent pacing.
 - Complete heart block associated with IMI typically has narrow complex escape rhythm with rate ~50–60 bpm and can often be monitored carefully without insertion of temp pacemaker unless there is hemodynamic compromise.
 - Heart block associated with Ant MI (bifascicular or complete heart block) usually requires emergency temp pacemaker placement (asystole risk)

CARDIOMYOPATHY/SHOCK/HEART FAILURE Cardiomyopathies

Dilated CMP

- Defined as ventricular dilation with decreased contractility.
- Etiologies: ischemic, valvular, HTN, idiopathic, myocarditis: viruses (echovirus, coxsackievirus, HIV), bacterial, fungal, rickettsial, Chagas, giant cell, Toxic: alcohol, athracyclines, radiation, cocaine; Autoimmune: peripartum, collagen vascular disease, sarcoid; Metabolic: hypothyroid, pheochromocytoma, acromegaly, thiamine or selenium deficiency; tachycardia induced, familial
- Work-up: history, ischemia evaluation (stress test vs. angiography), labs (TFTs, iron studies, HIV, others?), cardiac MRI?, endomyocardial bx?
- Treatment: Standard heart failure therapy.

Hypertrophic CMP

- Inappropriate LV and/or RV hypertrophy
- Pathology: mutations in sarcomere encoding genes. Myofibril disarray on pathology.
- Pathophysiology:
 - Subaortic outflow obstruction: narrowed tract from hypertrophied septum and systolic anterior motion of the mitral valve. Worsened with increased contractility.
 - Mitral regurgitation due to SAM.
 - Diastolic dysfunction from increased chamber stiffness
 - Ischemia: small vessel disease and subendocardial ischemia
 - Arrhythmias
- Physical exam: systolic crescendo-decrescendo murmur that increases with emptying the LV (with Valsalva or standing).

- Studies:
 - ECG: LVH, Q waves, large t-wave inversions.
 - Echo: severe LVH, SAM, significant MR.
 - MRI: hypertrophy and patchy delayed gadolinium enhancement
 - Catheterization: subaortic LV pressure gradient; Brockenbrough-Braunwald-Morrow sign: decrease in pulse pressure post extrasystolic beat.
- Treatment:
 - Drug therapy to reduce inotropy, palpitations (b-blockers, CCBs, disopyramide). Maintain adequate intravascular volume. If refractory with obstruction, surgical myomectomy vs. alcohol septal ablation.
 - ICDs to prevent sudden death if high risk.
 - Family counseling and genetic screening.

Restrictive CMP

- Impaired ventricular filling due to decreased compliance.
- Etiology: idiopathic fibrosis, autoimmune (scleroderma, polymyositis/dermatomyositis), infiltrative diseases (amyloid, sarcoid, hemachromatosis), storage diseases (Fabry's, Gauchers, etc.), Loffler's endocarditis, radiation, anthracyclines, serotonin (carcinoid, drugs), metastatic cancer
- Pathology: decreased myocardial compliance → normal EDV, but increased pressure → increased filling pressures
- Exam: elevated JVP, Kussmaul's sign, S3/S4, MR/TR. Congestive hepatopathy, ascites, edema.
- Diagnostic Studies:
 - Echo: LVH, atrial enlargement, significant diastolic dysfunction
 - Cath: atria: prominent x and y descents; Ventricles: dip and plateau. Concordance of LV/RV pressures during respiratory cycle (compared to restriction with discordance).
 - Treatment: volume control. Maintain sinus rhythm. Treat underlying condition.

VALVE DISEASES

Mitral Stenosis

- Etiology: mostly rheumatic (~80%) > other (endocarditis, mitral annular calcification, myxoma, thrombus, autoimmune valvulitis)
- Pathophysiology: elevated LA pressure, pulmonary HTN, AF
- Exam: high pitched opening snap, low pitched diastolic rumble, loud S1, presystolic accentuation (if in sinus rhythm).

Spectrum of Disease in Mitral Stenosis				
Stage	Mean Gradient (mm Hg)	PA Systolic Pressure (mm Hg)	Valve Area (cm²)	
Normal	0	<25	4–5	
Mild	<5	<30	1.5-2	
Moderate	5–10	30-50	1–1.5	
Severe	>10	>50	<1	

• Treatment: indicated in moderate-severe MS with symptoms or pulmonary HTN. Percutaneous

valvulotomy preferred if valve anatomy is amenable and there is not significant MR already. Otherwise surgery.

• Medical management: sodium restriction, b-blockers or calcium channel blockers to slow HR and allow for adequate LV filling, anticoagulation for large LA or AF.

Mitral Regurgitation

- Etiology: functional vs. structural
 - Structural: myxomatous degeneration (MVP), endocarditis, rheumatic, valvulitis, congenital, anorectic drugs
 - Functional: dilated CMP and annular dilation or papillary muscle displacement, ischemic papillary dysfunction, ruptured chordae
- Clinical: acute \rightarrow pulmonary edema, hypotension; chronic \rightarrow DOE, orthopnea, PND, AF.
- Exam: holosystolic murmur at apex, radiates to axilla, increases with handgrip, and decreased with Valsalva.
 - Anterior leaflet abnormality: murmur heard at spine
 - Posterior leaflet abnormality: murmur heard at sternum
- Treatment:
 - Acute MR: vasodilators, inotropes, IABP. Often need urgent surgery
 - Chronic MR: surgical repair better than replacement if possible. Indications if symptomatic or asymptomatic if EF < 50% and LV dilation, pulmonary HTN, or new AF.

Aortic Stenosis

- Etiology: Calcific (most common in >70 yrs), bicuspid valve (most common <70 yrs), rheumatic (usually with AI).
- Pathophysiology: increased afterload from pressure overload causes concentric hypertrophy
- Clinical: angina, syncope, heart failure, acquired vWD in approx 20% (Heyde's syndrome).
- Natural history: slowly progressive, but may have a rapidly progressive course as severity progresses (especially in calcific degenerative etiology). Need for AVR becomes urgent once symptoms develop in setting of severe obstruction Angina 5 yr mean survival; Syncope 3 yr mean survival; heart failure 2 yr mean survival.
- Physical exam: harsh systolic crescendo-decrescendo murmur at upper sternal border; radiates to sternal notch, carotids, apex (where it can sound like MR = Gallavardin effect).
 - Murmur increases with leg raise, decreases with Valsalva or standing.
 - Ejection click heard in bicuspid valve.
 - Signs of severity: late-peaking murmur, loss of A2, small and delayed carotid upstrokes (parvus et tardus).

Spectrum of Disease in Aortic Stenosis			
Stage	Mean Gradient (mm Hg)	Valve Area (cm²)	
Normal	<5	3.0-4.0	
Mild	<25	>1.5	
Moderate	25-40	1.0-1.5	
Severe	>40	<1.0	

Treatment

• Preferred treatment is surgical AVR for symptomatic AS or asymptomatic severe AS with

decreased EF.

- Percutaneous valve replacement available in Europe and in trials in the US.
- Medical management: gentle diuresis. Avoid venodilators and negative inotropes.
- Balloon aortic valvuloplasty (BAV): ~50% increase in AVA, but ~50% restenosis rate at 6–12 mo. Often used as bridge to AVR or through another complicated illness.

Aortic Insufficiency

- Etiology: leaflet abnormalities (bicuspid valve, endocarditis, rheumatic) or root dilation (HTN, aortic aneurysm/dissection, Marfan's, syphilis)
- Pathophysiology: volume challenge and increased LVEDP causes ventricular dilation
- Clinical manifestations: angina, orthopnea, dyspnea, left heart failure
- Exam: increased pulse pressure, early diastolic murmur (often with crescendo-decrescendo systolic murmur, many eponymous signs that are not associated with prognosis
- Echo: severity based on size of regurgitant jet and presence of flow reversal in descending aorta. Also assesses LV size and function.
- Treatment:
 - Acute: surgery usually urgently/emergently needed as it is poorly tolerated. Start therapy with IV
 afterload reduction (nitroprusside) and inotropes. Increased HR is better as less time for
 diastolic regurgitation.
 - Chronic: risks of progression to symptoms and LV dysfunction are both related to LV dimensions.
 - Surgery: symptomatic severe AI, asymptomatic severe AI and EF < 50% or LV systolic diameter >55 mm or diastolic diameter >75 mm, asymptomatic severe AI undergoing other cardiac surgery.
 - Medical therapy: vasodilators (ACE-I, nifedipine, hydralazine/nitrates)
 - Acute AI: often aortic dissection or endocarditis. Urgent surgery usually required. Until surgery, need afterload reduction, but do not use IABP.

Prosthetic Valves

Mechanical

- Bileaflet (St. Jude) tilting discs, ball, and cage.
- Very durable (20–30 yrs), but thrombogenic and require anticoagulation.
- Consider in younger patients (<65 yrs) or if already have indication for anticoagulation

Bioprosthetic

- Bovine pericardial or porcine heterograft, homograft
- Less durable, but minimally thrombogenic. Do not require anticoagulation.
- Consider in older patients or if contraindication to anticoagulation.
- Exam: crisp valve closure sounds (louder with mechanical valves). Soft flow murmur though prosthesis due to small, normal pressure gradients. Worrisome if absent sounds or regurgitant murmurs.
- Anticoagulation: even with warfarin, 1%–2% risk VTE yearly. Risk MVR > AVR and risk is highest early after implantation before endothelialization.
 - Warfarin: low risk mech AVR: INR 2–3 (consider 2.5–3.5 for first 3 mo); mechanical MVR or high-risk AVR(with prior VTE, AF, low EF, hypercoagulability): INR 2.5–3.5.

- ASA for bioprosthetic valves alone and with warfarin in mechanical valves is helpful.
- Bridging: warfarin should be stopped 48–72 hrs early with IV UFH when INR < 2 until 4–6 hrs before surgery; post-op restart UFH and warfarin ASAP.

PERICARDIAL TAMPONADE (JAMA. 2007;297:1810)

- Definition: hemodynamic insufficiency caused by cardiac compression due to fluid trapped in the pericardial space.
- Etiologies: pericarditis, iatrogenic, malignancy, idiopathic, MI, ESRD, CHF, collagen vascular disease, TB, other infections
- Pathophysiology: increased pericardial pressure → compression of heart → decreased venous filling → decreased cardiac output.
 - Diastolic pressures elevated in all chambers and equalize
- Diagnosis and clinical assessment:
 - Sign/sx: dyspnea, tachycardia, increased pulsus paradoxus, elevated JVP, hypotension (Beck's triad: hypotension, JVD, quiet heart sounds).
 - Pulsus paradoxus: exaggeration of normal respiratory ventricular interdependence causing decreasing LV stroke volume with inspiration. If >10 mm Hg, consistent with tamponade. Many conditions can have elevated pulsus paradoxus (severe lung disease and increased work of breathing, PE, hypovolemia, ascites).
- Diagnostics:
 - ECG: low voltage, electrical alternans; CXR with large cardiac silhouette
 - Echocardiogram: pericardial effusion, dilated IVC, septal shift, diastolic chamber collapse, respirophasic changes in transvalvular velocities.
 - Treatment: volume and inotropes, then pericardiocentesis.

Pericardiocentesis (Critical Care Clinics. 1992;8:699)

Indications

• Treatment for clinically significant pericardial tamponade

Contraindications/Considerations

- Uncorrected bleeding diatheses in nonemergent setting
- Always have cardiac surgical backup

Complications

• Atrial or ventricular puncture, atrial or ventricular laceration, cardiac arrhythmias, vasovagal reaction, pneumothorax, gastric or bowel perforation, acute pulmonary edema

CARDIOGENIC SHOCK AND TAILORED HEART FAILURE THERAPY

Shock

Hemodynamic Profiles of Shock				
Subtype	CVP	PCWP	CO/CI	SVR
Hypovolemic	Low	Low	Low	High
Cardiogenic	High	High	Low	High
Distributive (Septic/Anaphylactic)	Low	Low	Normal/high	Low
RHF or PE	High	Low to normal	Low	High
Tamponade	High	High	Low	High

PA Catheters (see Chapter 2)

- Rationale:
 - C.O. = $SV \times HR$. Stroke volume depends on preload (LVEDV) and afterload (SVR).
 - LVEDV is not easily measureable. However, using a balloon tipped catheter and measuring pressure beyond the balloon tipped when balloon is wedged in PA gives PCWP.
 - With no flow, PCWP = alveolar pressure = LA pressure = LVEDP, which is proportional to LVEDV. PA diastolic pressure will equal PCWP if no obstruction from PA to LA (e.g., arteriolar constriction, severe bronchoconstriction leadings to arteriolar constriction)
 - Assumptions fail when:
 - Catheter tip in area where PCWP does not equal alveolar pressure (if not in West lung zone 3)
 - Obstruction between PCWP and LV: mediastinal or lung fibrosis, PS, MS.
 - Abnormal compliance of LV so that LVEDP is not proportional to LVEDV
- Common uses of PA catheters:
 - Narrowing DDx: type of shock, mechanism of pulmonary edema, RV vs. LV failure
 - Diagnosis: pulmonary HTN, restrictive cardiomyopathy, tamponade, intracardiac shunt, MR/TR
 - Management: volume status, pressors, cardiogenic shock, complicated MI, post cardiac/thoracic surgery, pHTN
- Complications of PA catheters: RBBB, ventricular arrhythmia, PA rupture, pulmonary infarct, infection, catheter knotting.
- Efficacy:
 - No routine benefit to PAC in high risk surgery or ARDS (NEJM. 2006;354:2213).
 - No benefit for tailored heart failure therapy for decompensated CHF (JAMA. 2005;294:1625).
- Placement and Waveforms: see Chapter 2
- Cardiac output: can be measured using Fick equation or thermodilution.
 - Thermodilution: saline injected into RA. Change in temp over time measured at distant thermister is integrated. Inaccurate if low CO or severe TR.
 - Fick method: oxygen consumption = $CO \times arterio$ -venous (AV) oxygen difference
 - CO (l/min) = oxygen consumption (l/min)/[(AVO₂ difference)(10)(1.34 ml/g)(Hgb g/dl)].
 - Can estimate oxygen consumption using weight based formulae, but best to measure.
- Resistances:
 - SVR = (MAP RA)/CO
 - PVR = (PA mean PCWP)/CO
 - 1 wood unit = $80 \text{ dyne/(cm} \times \text{sec}^5)$
- Hemodynamic considerations:
 - All quantitative measurements should be made at end expiration.
 - Positive pressure ventilation inverts respirophasic variation (RA pressure increases with positive pressure inspiration).
 - Measure RA and PCWP at the end of diastole, i.e., at the end of the a wave.

Decompensated Heart Failure/Tailored Therapy

- Definitions/General Considerations:
 - Definition: dyspnea from rapid accumulation of fluid due to increased LVEDP
 - Precipitants: myocardial ischemia/infarction, dietary or pharmacologic non-adherence, uncontrolled HTN, arrhythmia, endocarditis, valvulopathy, tamponade, myocarditis, fluid overload, high output state (anemia, systemic infection, hyperthyroidism, etc.), toxins (EtOH,

- cocaine, etc.), iatrogenic (anthracyclines, steroids, etc.), infection
- Most common hospitalizing diagnosis.
 - Low output (decreased CO) vs. high output (increased SV, increased CO)
 - Left heart failure (pulmonary edema/congestion) vs. Right heart failure (JVD, edema, ascites, hepatomegaly
 - Systolic (insufficient CO so cannot perfuse organs) vs. Diastolic (impaired ventricular filling)

History, Exam, Labs, Radiographs

	4 Major Hemodynai	mic Profiles	
	No Congestion	Yes Congestion	
Adequate perfusion (warm)	"Warm and dry" Outpt management	"Warm and wet" Majority of patients Rx with diuretics =/- vasodilators	
Low perfusion (cool)	"Cool and dry" Rx with (ICU)	"Cool and wet" Rx with inotropes and vasodilators; tailored and advanced therapy (ICU)	

(JACC. 2003;41:1797)

- Evidence for low perfusion: narrow pulse pressure, pulsus alternans, cool forearms and calves, drowsy/obtunded, poor tolerance of ACE-I and b-blockers, hyponatremia, worsening renal function
- Evidence for congestion:
 - Left-sided: dyspnea, orthopnea, PND, S3, rales
 - Right-sided: elevated JVP, loud P2, right sided S3, increased TR, edema, ascites, anorexia, HJR
- RA pressure in mm Hg = JVP (in cm water)/1.3
- CXR signs: pulmonary edema, pleural effusions (L > R), cardiomegaly.
- BNP (or its isoforms): useful when diagnosis is uncertain

Adduses		Volume		Optimize
Address Etiology	Hemodynamics	Volume Status	Oxygenation	Chronic Therapy
 Treat precipitant and etiology (such as ischemia, arrhythmia, etc.). Address lifethreatening conditions (STEMI, malignant arrhythmias, etc.) 	 Vasodilators to decrease afterload Inotropes if low output (may need to cut or stop β-blockers during acute decompensation) 	Sodium restriction IV diuretics initially give predictable bioavailability May need combination of loop and thiazide diuretics for multiple mechanisms Convert to oral diuretics when able Follow daily weights and I/Os.	 Oxygen Morphine decrease work of breathing and some venodilation May need NIPPV, or eventually, mechanical ventilation 	 Transition once stable of IV agents and euvolemic Move toward long agents with evidence (ACE-I/ARE β-blockers, aldosterone antagonists, etc.)

Heart Failure with Preserved EF (Diastolic Heart Failure)

- DDx: HTN/LVH, HCMP, infiltrative CMP (amyloid, hemachromatosis, sarcoid, etc.), restriction, scar, non-compaction
- Findings: S4, LVH, normal EF on echocardiogram
- Treatment goals:
 - No specific evidence-based treatment, address underlying etiology
 - Optimize volume and reduce congestion
 - Rhythm control: prevent tachycardia, prolong diastole, and maintain sinus rhythm (to preserve atrial kick)

Cardiogenic Shock/Tailored Therapy

- Cardiogenic shock definition: SBP < 80 mm Hg, CI < 2.2 1/min/m², PCWP > 18 mm Hg
- Tailored therapy with PA catheter to guide treatment based on hemodynamics.
- Tailored therapy: reduce congestion while increasing CO and preserving MAP.
 - Goal is to measure LVEDP. However, LVEDP cannot be measured without left heart catheterization. Thus PA catheterization allows measurement of PCWP. If many assumptions are made: LVEDP = LAP = PCWP (inaccurate if valvular disease, lung disease).
- Hemodynamic goals of tailored therapy: MAP > 60 mm Hg, CI > 2.2, PCWP 14–18 mm Hg, CVP 8–12 mm Hg, SVR < 800.

Approach to Tailored Therapy				
Fluid (Preload) Optimization	SVR (Afterload) Optimization	CI (Inotropy) Optimization		
 PCWP high: diuresis +/- inotropes PCWP low: crystalloid or colloid Many patients in cardiogenic shock have low PCWP and need fluid. Clues to hypovolemia include hypotension on positive pressure ventilation and pulse pressure variation. Consider higher PCWP goals in LVH, HOCM, infiltrative disease 	 SVR > 1,200: vasodilators such as nitroprusside Occasionally in patients with increased SVR, vasodilators actually raise the MAP. Besides vasodilators, an IABP also lowers SVR. 	If CI < 2.2: try to augment CI by optimizing PCWP and SVR. If still not at goal, may need inotropes		

PACEMAKERS AND DEFIBRILLATORS

Pacemaker Nomenclature

- Single chamber PPM: RV lead only.
- Dual Chamber PPM: when atrial-ventricular synchrony still possible. RA and RV lead.
- Cardiac resynchronization therapy (CRT) (also called Bi-ventricular PPM): RV and LV lead (in cardiac veins). Indicated in heart failure with wide native QRS.

A: atrial,		ker Codes: tion, D: dual, R: rate-n	nodulation	
1st Letter 2nd Letter 3rd Letter 4th Letter				
Chamber(s) paced	Chamber(s) sensed	Response to sensing	Rate modulation	

Common Examples

- VOO: asynchronous ventricular pacemaker. Magnet placed over permanent PPM reverts to VOO (or occasionally DOO).
- VVI: ventricular demand pacing; output in ventricle inhibited by sensed native QRS complex in ventricle. Mode used in temporary pacing.
- DDDR: Most common mode for permanent dual chamber devices. For chronotropic incompetence/AV block. Allows AV synchrony if the native complexes are not too bradycardic or conducted too slowly. Rate responsive to increase HR with activity.

Indications for Permanent Pacing (PPM) (Circ. 2008;117:2820)

- Symptomatic bradycardia in general.
- AV block: symptomatic 3rd or 2nd degree block. Asymptomatic 3rd degree block or type II 2nd degree block is questionable.
- Sinus dysfunction: Sinus bradycardia or pausing with sxs. Chronotropic incompetence.

Indications for Temporary Pacing

- Generally the same indications as for PPM
- Symptomatic bradycardias (such as sinus brady, acquired AV block, post-MI, syncope). Variable progression to PPM depending on if indication is permanent.
- Most common situations for temporary pacing that do not require PPM:
 - Acute bradycardia or AV block: post-surgical or traumatic conduction system disease, Lyme, toxic, medication, endocarditis, peri-procedural (alcohol septal ablation, etc.).
 - Overdrive pacing: for recurrent polymorphic VT to prevent R on T phenomena.
 - Acute MI and conduction block.

Cardiac Resynchronization Therapy (CRT)

- Pacing of both ventricles (via RV lead and coronary sinus lead for LV) with goal of restoring ventricular-ventricular synchrony.
- Indications for CRT: class III/IV ischemic and non-ischemic CMP despite optimal therapy. EF < 35%, QRS > 140 ms or >120 ms with evidence of dyssynchrony.

Implantable Cardioverter-Defibrillators (ICDs) (NEJM. 2008;359:2245)

- Goal: to terminate VT/VF with burst pacing or shock and prevent sudden death.
- Unlike PPMs, ICDs are programmed for bradycardia and tachycardia.
- Most often, if ICD senses tachyarrhythmia there are several responses: anti-tachycardia pacing to attempt to terminate rhythm without shock or series of shocks.
- Indications for ICD:
 - Secondary prevention: survivors of VT/VF arrest, unstable VT/VF without reversible cause, structural heart disease, and VT.
 - \bullet Primary prevention: life expectancy >1 yr, LVEF < 30% or LVEF 30%–35% and NYHA II-III or

LVEF 35%–40% and inducible VT/VF. Also for HCMP, Brugada, sarcoid, Long QT, Chagas, congenital heart disease with risk factors.

Device Complications

- Acute: tamponade, hematoma, pericarditic pain, PTX.
- Later Complications:
 - Failure to pace: from battery failure, lead fx/dislodgement, increased pacing threshold.
 - Failure to sense: from lead dislodgement or increasing thresholds
 - PPM mediated tachycardia: reentrant tachycardia initiated by early beat conducted retrograde where it is sensed and triggers paced beat, thus causing reentrant circuit.
 - PPM syndrome: palpitations, heart failure from loss of AV synchrony or × synchrony.
 - Device infection: pocket infection or lead infection requiring removal of system.
 - Inappropriate shocks: can cause serious psychiatric distress. Place magnet over system.

PHARMACOLOGY OF CV DRUGS (SEE CHAPTER 25)

Inotropes and Vasopressors

Drug	alpha	beta-1	beta-2	dopa	Other	CO/CI	SVR	MAP	HR
Dopamine (low dose)	none	none	none	wk	none	wk	none	none	wk
Dopamine (medium dose)	wk	strong	wk	wk	none	medium	none	none	wk
Dopamine (high dose)	strong	strong	wk	wk	none	strong	strong	strong	strong
Epinephrine	strong	strong	strong	none	none	strong	strong	strong	strong
Phenylephrine	strong	none	none	none	none	decrease	strong	strong	none
Isoproterenol	none	strong	strong	none	none	wk	decrease	none	strong
Vasopressin	none	none	none	none	V1,V2	none	strong	strong	none

Inotropes

- Generally used in decompensated heart failure/cardiogenic shock.
 - Milrinone: phosphodiesterase inhibitor. Causes increased inotropy, modest vasodilation. BP effect is variable. Some pulmonary vasodilation. Pro-arrhythmic.
 - Dobutamine: non-selective beta agonist. Increased inotropy/chronotropy. Less vasodilation than milrinone. BP effect variable. Also pro-arrhythmic.

Antihypertensives

Beta-blockers

- Mechanism via inhibition of beta receptors on cell surface.
- Uses: HTN, angina, chronic systolic heart failure, rate control, antiarrhythmics
- Multiple classes based on mechanism:
 - Beta-1 selective: metoprolol, atenolol, etc.
 - Non-selective: nadolol, propranolol
 - Combined alpha and beta blockers: carvedilol, labetalol
- Miscellaneous: carvedilol, bisoprolol, metoprolol (sustained release) improve mortality in chronic systolic heart failure.
- Side effects: hypotension, bradycardia/heart block, negative inotropy, fatigue/lethargy, sexual impotence.

Calcium Channel Blockers

- Two classes: dihydropyridines and non-dihydropyridines
 - Dihydropyridines: amlodipine, nifedipine, etc. Function peripherally. Use in HTN, coronary spasm/Reynaud's, PAH. Adverse reaction: LE edema.
 - Non-dihydropyridines: verapamil, diltiazem. Function at level of heart, but also lower BP. Use as anti-anginals, rate controlling agents. Adverse reactions: negative inotropes, heart block/bradycardia, hypotension.

Angiotensin Converting Enzyme Inhibitors (ACE-I)/Angiotensin Receptor Blockers/Renin antagonists/Aldosterone antagonists:

- Interrupt renin—angiotensin—aldosterone system at different levels.
- Cause small decrease in GFR and increase serum potassium.
- Uses: HTN, post-MI, chronic heart failure, prevent progression of renal disease
- Adverse reactions: renal failure, hyperkalemia, hypotension, cough (ACE-I only, not ARBs or aldo antagonists). Avoid ACE-I in bilateral renal-artery stenosis.

Nitrates

- Administered in many ways (PO, SL, transdermal, IV).
- Venodilators and anti-anginals.
- Uses: angina, HTN (although much more powerful on venous dilation than arterial dilation), vasospasm.
- Adverse reactions: hypotension, headache. Tolerance achieved quickly.

Diuretics

- All cause natriuresis. Can be used in conjunction with each other if different classes.
- Thiazides (HCTZ, chlorthalidone, metolazone, etc.): function in proximal nephron.
- Loops (furosemide, bumetanide, torsemide, etc.): function at Loop of Henle
- Carbonic anhydrase inhibitors: acetazolamide

Alpha-Blockers

- Used for HTN, BPH. Particularly useful in pheochromocytoma.
- Adverse effects: orthostatic hypotension. Central effects.

Others

- Nitroprusside: direct arterial dilator. Most effect anti-HTN. Cyanide or thiocyanate toxicity with prolonged use (more rapidly if liver or kidney dysfunction.)
- Hydralazine: direct arterial dilator. Anti-HTN. Decreases mortality in combo with nitrates in heart failure. Can cause auto-immune reaction.
- Clonidine: centrally acting alpha agonist. Rebound HTN with withdrawal.

ANTIPLATELETS/ANTICOAGULANTS

Antiplatelets Agents

- Different mechanisms in preventing platelet activation/aggregation. Primary adverse effect of all agents is bleeding.
- ASA: Mechanism: Irreversibly blocks thomboxane A2 mediated platelet aggregation via actions on COX enzymes.
 - Used in stable atherosclerosis (CAD, PAD, stroke prevention), ACS, post-PCI.
 - Long functional half-life.
- Thienopyridines: clopidogrel, prasugrel. Irreversible ADP receptor antagonists. Oral administration. Require loading dose. Used in ACS, post-ACS, post-PCI, CVA prevention.
- GP IIb/IIIa inhibitors: IV infusions. Three agents available. Use in ACS and to facilitate PCI.
- Ticagrelor: reversible P2Y₁₂ receptor antagonist. Use will be in ACS, post-PCI. Short half life.

Antithrombotics

- All balance benefit of anticoagulation with risk of bleeding.
- Heparins: UFH/LMWH. Available IV (UFH) or as subcutaneous injection (LMWH). Useful in atrial fibrillation, ACS, facilitating PCI, venous thromboembolism, mechanical valves.
 - UFH requires titration to aPTT. Reversible with protamine. Short half-life (90 min).
 - LMWH generally needs no titration. Wt-based dosing. Contraindicated in renal failure. Can be monitored with anti-Xa levels. Not reversible and longer half-life. Can be self-administered.
 - All associated with HIT.
- Warfarin: Inhibits vitamin K dependent clotting factor (II, VII, IX, X) generation.
- Oral. Requires aPT (INR) monitoring. Slow to become therapeutic.
- Thrombin inhibitors:
 - IV agents: argatroban, bivalirudin, hirudin, lepirudin
 - Oral agents becoming available: dabigatran
 - Can be used in place of heparins or to treat HIT.

Antiarrhythmics

Vaughan-Williams classification created 4 classes of antiarrhythmics.

- Class I agents: sodium channel blockers.
- Class II agents: beta-blockers
- Class III agents: potassium channel blockers
- Class IV agents: calcium channel blockers

Commonly Used ICU Antiarrhythmics (also see Appendix and Chapter 14)

- Amiodarone: class 3 agent. Long half life. Useful with atrial and ventricular arrhythmias. Most effective agent for maintaining sinus rhythm in atrial fibrillation/flutter. IV or PO available. IV formulation has more b-blocker properties. Causes thyroid, liver, lung, eye toxicity. Typical load for VT/VF is 8–10 g cumulative before switching to maintenance dosing (4–5 g for atrial dysrhythmias).
- Lidocaine: class Ib agent. Useful for VT (particularly ischemic VT or post-MI). IV formulation. Hepatic metabolism and renal excretion. Levels should be monitored. Toxicity includes non-specific CNS effects, and eventually seizures.
- Procainamide: class Ib agent. Particularly useful if in bypass tract-dependent arrhythmias (WPW).
- Sotalol: combined Class II/III (b-blocker/potassium blocker). Useful for VT and atrial fibrillation. Needs careful QTc monitoring.
- Ibutilide: class III agent. Particularly useful for chemical cardioversion from atrial fibrillation. Pretreat with magnesium. Monitor QTc.

CARDIAC SURGICAL CRITICAL CARE

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COMMON POST-OPERATIVE MANAGEMENT ISSUES

Bleeding

- Diff. diagnosis: surgical bleed; thrombocytopathia and thrombocytopenia; inadequate heparin reversal; DIC vs. primary fibrinolysis; coagulopathy secondary to hypothermia
- Diagnostic techniques: check drain output; examine for localized vs. diffuse bleeding; serial CBC; PT/aPTT/INR; TEG; ACT; fibrinogen and D-dimers, core temperature.

Hypotension

- Diff. diagnosis: cardiac tamponade; hemothorax; tension PTX; arrhythmias; myocardial ischemia (inadequate cardioplegia and cardioprotection, incomplete revascularization, reperfusion injury, etc.); electrolyte abnormalities; hypovolemia; bleeding; hypoxemia; acidosis (metabolic or respiratory); acute coronary graft closure.
- Diagnostic techniques and interventions: CXR; 12-lead EKG; CBC; chem 10; ABG; TTE immediate bedside sternotomy if caused by cardiac tamponade; immediate needle decompression or chest tubes to suction if caused by tension PTX (have absent breath sounds; tracheal deviation).

Hypertension

- Diff. diagnosis: emergence from anesthesia; inadequate analgesia; volume overload; electrolyte abnormalities (low glucose); hypothermia; hypoxemia/hypercarbia (sympathetic stimulants)
- Diagnostic techniques: post-operative pain management and sedation; ABG; FSBG; core temperature

Arrhythmias

- Diff. diagnosis: myocardial ischemia (incomplete revascularization, incomplete cardiac protection, etc.); electrolyte abnormalities (esp K, Mg); new AV conduction abnormalities due to valve suture placement; hypothermia; CVC/PA placement; hypoxemia/hypoventilation; acidosis.
- Diagnostic techniques: 12 lead EKG (afib is the most common dysrhythmia); chem 10; check pt's core temperature; CXR for central venous catheter position; ABG; check epicardial pacer settings

Alteration of Mental Status

- Diff. diagnosis: CNS emboli/new CVA; neurocognitive dysfunction; residual anesthetic; delirium; electrolyte abnormalities and hypoglycemia; infection; hypoxemia/hypercarbia
- Diagnostic techniques: head CT; delirium screen; chem 10; ABG

Respiratory Failure (Hypoxemia, Hypoventilation)

• Diff. diagnosis: reperfusion injury for (lung transplant); atelectasis; mucus plugging; PTX; pulmonary edema from mobilization of fluids; respiratory insufficiency 2/2 damaged phrenic

and/or recurrent laryngeal nerves; PE

• Diagnostic techniques/treatment: ABG; CXR; aggressive pulmonary toilet and bronchodilators; diuresis as needed; pain management; chest tube placement

Renal Failure

- Diff. diagnosis: pre-renal (perioperative hypotension; inadequate CO; hypovolemia); CPB (nonpulsatile flow); hemolysis-associated tubular injury; ATN; Ao cross-clamp placement (higher incidence with supra-renal clamps); contrast nephropathy; immunosuppressant (e.g., cyclosporine) nephrotoxicity
- Diagnostic techniques: monitor UOP; UA with micro; FeNa or FeUrea; BUN/Cr

Paraplegia: (Following Repair of Thoraco-Abdominal Aneurysm or Dissection)

• Diff. diagnosis: anterior cord syndrome due to inadequate perfusion; epidural hematoma; accidental intrathecal placement of epidural catheter

EXTRA-CORPOREAL ASSIST DEVICES

Extracorporeal Life Support (ECLS)

Indications

• Severe, acute, reversible cardiac, and/or pulmonary failure refractory to conventional medical management

Relative Contraindications: ("General Guidelines for all ECLS Cases." 2009)

- Pre-existing conditions expected to impact quality of life severely or to prevent a normal life even after successful ECLS
- Age/size of patient: no absolute cut-offs but increasing risks at the extremes of futility

Equipment/Components

- Cannula:
 - One cannula/lumen for blood removal and one cannula/lumen for blood return
 - Can be placed centrally (e.g., right atrium and aorta) or peripherally (e.g., femoral artery and vein)
 - Cannula diameter and length determines resistance to flow, and therefore, maximum blood flow through the circuit
- Circuit transportable, closed to the atmosphere, smaller than standard cardiopulmonary bypass circuits
 - Membrane lung oxygenator oxygenates and removes CO2 from the blood
 - Heat exchanger actively warms or cools blood
 - Pump provides centrifugal, non-pulsatile flow
 - Monitors, alarms continuous monitoring of flow and rotations per min (rpm)

	Modes of Perfus	ion
	Veno-Veno (V-V)	Veno-Arterial (V-A)
Anatomy	Blood removed and returned to venous system	Blood removed from vein and returned to an artery
Blood pressure	Determined by native cardiac output and SVR	Determined by pump flow and native SVR
Oxygenation	Yes, can provide full support	Yes, can provide full support
CO ₂ removal (ventilation)	Yes, can provide full support	Yes, can provide full support
Cardiac support	None	Yes, can provide full support

Common Terms and Definitions

- Rated flow: flow rate of venous blood (vO_2 sat 75%) that can be maximally oxygenated to a vO_2 sat 95% in a min, as measured at the membrane lung outlet
 - Flow rate of the membrane lung should be greater than the required flows for maximum patient support
 - Suspect a membrane lung problem if the post-membrane O_2 sat < 95% at flows < rated flows
- Sweep gas: gas applied to the membrane oxygenator
 - Commonly O_2 or carbogen (95% O_2 + 5% CO_2)
 - Sweep gas rate controls CO₂ clearance
- Priming solutions: solution used to fill the circuit prior to cannulation
 - Commonly crystalloid, albumin, or PRBCs

To patient

From patient

To patient

Note that the patient of the patient

Figure 1. Example of V-V and V-A Cannulation

Management: ("Patient Specific Supplements to the ELSO General Guidelines." 2009)

- Anticoagulation:
 - Heparinize (50–100 units/kg) for cannula placement
 - Heparin gtt to maintain ACT $> 1.5 \times normal$
- Ventilator settings:
 - Oxygenation and ventilation primarily accomplished by the membrane lung

- Follow pre- and post-membrane lung gases
- Ventilator settings should focus on resting the lung, especially in patients with respiratory failure or inflammation → low RR, plateau < 30, FiO₂ < 0.3, PEEP to prevent atelectasis without compromising venous return
- If possible, allow spontaneous respirations

	V-V	Peripheral V-A	Central V-A			
Anatomy	Returned oxygenat- ed blood enters venous system and mixes with systemic deoxygenated venous blood	Returned oxygenated blood flows retrograde from femoral artery and mixes in the mid aorta with desaturated systemic blood pumped through the native heart	Returned oxygenated blood flows into proximal aorta			
Expected SaO ₂	If little or no native lung function, expect $SaO_2 \ge 80\%$ and $SvO_2 > 70\%$	Variable, depending on where mixture in the aorta occurs and where blood is sampled	Close to 100%			
Special Due to the lower expected SaO ₂ , must maintain adequate CO and Hct for sufficient tissue oxygen delivery		Beware of inadequate oxygenated perfusion of coronary and cerebral arteries. Expect more proximal aortic mixing with higher pump flows.	Knowing cannula location is critical. Unusual cannula placements can affect management in emergencies (e.g., cardiac arrest in a PA – Ao cannulated patient → R heart support for adequate pre-load is essential!			

- Sedation and neurologic monitoring:
 - Minimize sedation once stable on ECLS for frequent neurologic monitoring given risk of embolic and hemorrhagic CNS events
- Prophylactic antibiotic use:
 - No consensus regarding routine antibiotic prophylaxis regimens; institution-dependent.
- Fluid management:
 - Initiate diuresis or CRRT to maintain dry body weight and euvolemia
- Weaning:
 - Start weaning trials once the required cardiac and/or pulmonary support provided by ECLS is <30%
 - Method of weaning highly variable depending on type of ECLS support and underlying disease

Common Problems					
	V-V	Peripheral V-A	Central V-A		
Hypotension	Hypovolemia Pneumothorax Cardiac tamponade Low SVR Low native CO.	Low pump flow. Hypovolemia (look for circuit "chugging"). Cannula malposition. Cardiac tamponade. Pneumothorax. Low SVR.	Same as peripheral V-A		
Hypertension	High SVR state	High SVR state — consider adding vasodilators (e.g., nitroprusside, esmolol, etc.). High pump flow Cannula malposition — measure at multiple sites, upper and lower extremity	Same as peripheral V-A		
Нурохіа	High native CO: higher blood flows through the native diseased lungs. Malfunctioning membrane lung (e.g., clotting). Required flows are greater than the membrane lung's rated flow. Low pump flows. Cannula malposition.	High adrenergic state – pain, agitation, iatrogenic (vasopressors) causing high native CO Cannula malposition – sample at multiple sites High native CO: results in more distal mixing of oxygenated and deoxygenated blood in the Ao. Can add an additional RA return cannula (V-V-A), change to central cannulation, ↑ pump flows, or ↓ native CO (e.g., esmolol gtt). Low pump flow. Hypovolemia. Membrane clotting.	High adrenergic state – pain, agitation, iatrogenic (vasopressors) causing high native CO. High native CO: consider adding agents to decrease native inotropy (e.g., esmolol gtt). Low pump flow. Membrane clotting.		
Hypercarbia	Malfunctioning membrane lung (e.g., clotting) High native CO Low pump flow	Same as V-V	Same as V-V		

• Hematologic:

- Bleeding: most common problem with ECLS
 - Minimize unnecessary procedures (e.g., venipuncture, ETT suctioning, etc.)
 - Ensure anticoagulation is within the appropriate range
 - If uncontrolled hemorrhage, can consider reversal of anticoagulated state with FFP, platelets and anti-fibrinolytics (e.g., Amicar) and turning off the heparin gtt but risk of circuit clotting increases.
- Thrombocytopenia:
 - Ddx: drug effect, underlying disorder, splenic/liver sequestration after platelet activation from exposure to the ECLS circuit, HIT
- Consider argatroban gtt if suspicion for HIT is high
- Hemolysis:
 - Causes: membrane inlet suction pressures > -300 mm Hg; pump clots; high flows through a

small return cannula; occlusions in the return circuit

- Circuit clotting:
 - No action required for clots <5 mm
 - Exchange circuit or replace the circuit section with the clot
 - Check ACT levels; consider AT3 deficiency and FFP transfusion for recurrent clotting despite appropriate heparin dosage
- Inadequate venous drainage:
 - Replace cannula with a larger cannula
 - Place additional venous cannula in a separate location
- Catastrophes:
 - Air entrainment or O₂ emboli: (1) stop pump and clamp cannulas/lines near the patient, institute support settings; (2) locate source of air entrainment (e.g., drainage vs. return line, membrane lung)
 - Check cannulation site of the drainage cannula for leaks
 - Check connectors and stopcocks in the circuit tubing
 - Check other IV lines in the patient
 - Keep systemic blood pressure greater than the sweep gas pressure; keep the membrane lung below patient level
 - Power failure:
 - Should automatically revert to the backup battery (30–60 min energy supply)
 - Turn off unessential, high-energy components of the circuit (e.g., heated water bath)
 - Identify cause of the power failure
 - If unable to restore power and/or battery fails, use the manual hand crank
 - Unintentional decannulation:
 - Stop pump, clamp lines close to patient, and apply pressure to the original cannulation site
 - Initiate backup ventilator settings
- Ischemic/embolic events:
 - Limb ischemia from peripheral cannulation
 - Coronary or cerebral ischemia from inadequate oxygenation with peripheral V-A ECLS
 - Inadequate flows for organ perfusion (e.g., renal failure)
 - Embolic events due to inadequate anticoagulation

VENTRICULAR ASSIST DEVICES (VADs) (Can J Cardiol. 1996;12(10):1017; A Practical Approach to Cardiac Anesthesia, 2008)

Indications: for severe cardiogenic shock and hemodynamic compromise as a:

- Bridge to cardiac recovery or transplantation
- Destination therapy for non-transplant candidates

Physiologic Benefits

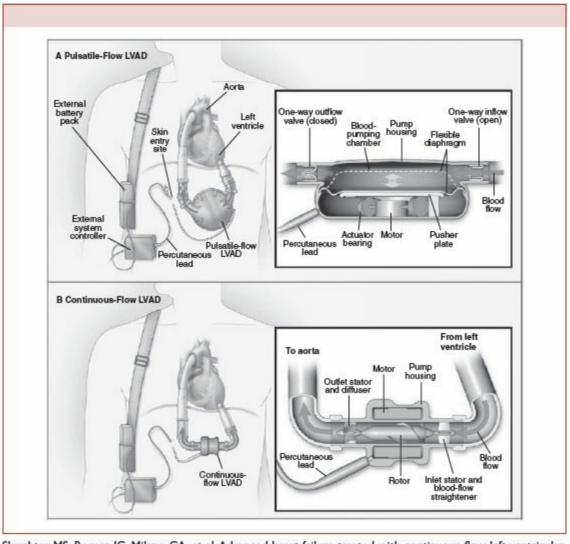
- ↓ myocardial work and O₂ consumption
- ↓ myocardial wall tension
- ↑ ventricular unloading
- ↑ CO

Components/Types

- Composed of cannulas (inflow cannula to the pump, outflow cannula returning blood to the patient), pump (pulsatile or continuous flow pumps), and a power supply
- Used in parallel to the native heart; does not require excision of the diseased ventricles, as with total artificial hearts (TAH)

	Types of VADs	
Types	Cannulation Sites	Notes
LVAD (LV ventricular device)	Inflow cannula: LV apex Outflow cannula: ascending aorta	LA can be cannulated for the inflow cannula for short-term therapy only given risk of LV thrombus formation from blood stasis
RVAD (RV ventricular device)	Inflow cannula: RA or RV Outflow cannula: pulmonary artery	Significantly lower risk of RV thrombus formation with RA cannulation
BiVAD (Biventricular device)	Combination of the LVAD and RVAD	Provides complete cardiovascular support

Figure 2. Example LVAD Devices



Slaughter MS, Rogers JG, Milano CA, et al. Advanced heart failure treated with continuous flow left ventricular assist device (N Engl J Med. 2009;361).

	Types of VAD Pumps		
Pump Type	Valves	Comments	Examples
Pulsatile (a) volume displacement	Inflow and outflow valves	More afterload insensitive.	Abiomed BVS 5,000. Heartmate XVE (Thoratec). PVAD/IVAD (Thoratec). Worldheart Novacor.
Continuous flow (a) axial flow (b) centrifugal flow	None	Pros: smaller, ?easier implantation Cons: No palpable pulses or arterial waveform (e.g., out of hospital arrest) w/ full support. Afterload sensitive; e.g., poor RVAD flow w/ ↑ PVR Poor pre-load can cause "device regurgitation" due to lack of valves	HeartMate II (Thoratec) Incor (Berlin Heart) Jarvik 2,000 (Jarvik Heart) CentriMag Hemopump Impella (see below)

PVAD - paracorporeal ventricular assist device; IVAD - implantable ventricular assist device.

Management

- Hematology:
 - Requires chronic systemic anticoagulation and antiplatelet therapy
 - Exception: HeartMate XVE device has a special anti-thrombotic surface
 - If transfusions are indicated for transplant candidates, consider leuko-reduced PRBCS to minimize alloantibody formation
- R heart function in LVAD patients:
 - Critical to maintain R heart function in LVAD-only patients
 - May require inotropes, chronotropes, systemic vasoconstrictors, and pulmonary vasodilators
- LVAD effect on valvular dysfunction or PFOs:
 - May worsen pre-existing AI by ↓ LVEDP from unloading in the setting of ↑ systolic BP (sBP)
 - May unmask or worsen PFOs (RAP > LAP w/ L-sided unloading)
- Arterial waveforms:
 - Arterial waveforms corresponding to EKG QRS in continuous flow VADs indicate native left ventricular function

Complications: (Ann Thorac Surg. 2009;88:1162)

- High cumulative incidence of ≥1 significant adverse event in the acute (<60 d) post-implantation period
- Early complications (POD 0–10):
 - Arrhythmias
 - Ventricular arrhythmias particularly common given ventricular insertion site
 - Replete electrolytes; consider anti-arrhythmic medications (e.g., amiodarone), cardioversion and ICD placement depending on the arrhythmia's effect on VAD filling.
 - Pre-existing ICDs should NOT be de-activated after LVAD or RVAD placement
 - Refractory malignant arrhythmias may require conversion to BiVAD
 - Tamponade
 - Significant bleeding
 - Renal/hepatic injury

- Late complications (POD 11–60)
 - Infection, neurologic events, thromboembolism, reoperation
 - Device malfunction: suspect with poor device flow and TEE/TTE evidence of an non-decompressed, cannulated ventricle
 - Right heart failure: in patients with LV support only; suspect with poor device flow and TTE/TTE evidence of a decompressed LV
 - *Note:* * = highest overall incidence

MINIMALLY INVASIVE INTERVENTIONS

Percutaneous VADs: (Cardiothorac Vasc Anesth. 2010;24(3):478) **Indications**

- Short-term (<14 d) therapy of cardiogenic shock
- Bridge to procedure (e.g., longer-term VAD placement)
- Cardiac support for complex percutaneous cardiac procedures

	Types of Percutaneous VEDs				
	Tandem Heart	Impella			
Anatomy and placement	Transseptal left atrial-to-femoral arterial device Inflow/drainage cannula inserted in the femoral vein → RA → transseptally → tip positioned in LA Outflow/return cannula inserted in the common femoral artery → advanced to common iliac artery	Femoral artery or R axillary artery insertion Positioned across the aortic valve with the distal inflow port in the LV and the proximal outflow port in the aorta Placed in cath lab			
Flow dynamics	Continuous, low-speed, centrifugal pump Non-pulsatile flow	Axial flow rotary pump Non-pulsatile flow			
Flow rates	Up to 4-5 I/min at 7,500 rpm	2 sizes (LP 2.5 and 5.0) that provide maximum 2.5 l/min or 5 l/min flows			
Anticoagulation	Systemic anticoagulation w/ heparin gtt	Systemic anticoagulation w/ heparin gtt			
Contraindications	Severe RV dysfunction or failure (when used as a L heart device) Severe Al VSD Severe PAD and/or femoral grafts Contraindications to anticoagulation IVC filter (relative)	Severely calcified AV +/- AS Prosthetic AV Severe Al Severe PAD			
Efficacy over IABPs	RCTs show no mortality benefit over IABPs (Thiele H, Eur Heart J. 2005; 26(13):1276; Burkhoff D, Am Heart J. 2006;152(3):469)	RCTs and meta-analysis showed ?improved hemody- namics but no proven mortality benefit compared to IABPs (Seyfarth M, J Am Coll Cardiol. 2008; 52:1584; Cheng JM, Eur Heart J. 2009; 30:2102)			
Complications	CVAs; vascular injury; limb ischemia; hemorrhage; hemolysis, thrombocyto- penia Catheter migration Paradoxical embolism: secondary to trans-septal approach Cardiac tamponade	CVAs; vascular injury; limb ischemia; hemorrhage; hemolysis, thrombocytopenia Catheter migration: LV overload if proximal port is too deep or aortic valve leaflets are unable to coapt cardiac tamponade			

Intra-Aortic Baloon Pump (IABP): ("Clinical Applications of the Intra-Aortic Balloon Pump." 1998) Indications

- Supports short-term LV failure refractory to maximum medical inotropic support (e.g., acute cardiogenic shock, failure to wean from intraoperative CPB, acute MI/unstable angina)
 - Temporizing measure until cardiac recovery or as a bridge to other procedures (e.g., transplant, complex/high-risk PTCA, VAD, etc.)
- Improves myocardial O₂ supply and demand balance
 - Improves coronary perfusion by diastolic augmentation (\uparrow dBP and \downarrow LVEDP) \rightarrow increases CPP
 - Coronary perfusion pressure (CPP) = dBP LVEDP
 - Systolic unloading: \downarrow MVO₂ by \downarrow systolic aortic pressure $\rightarrow \downarrow$ LV afterload and \downarrow LVEDP

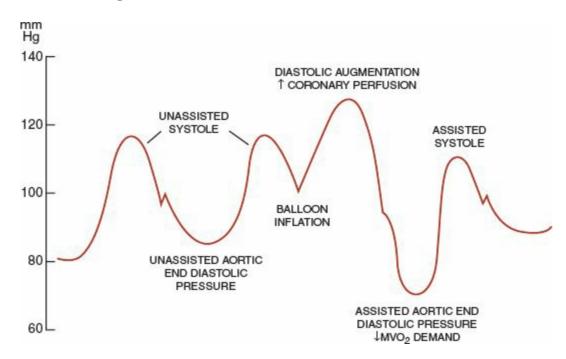
Relative Contraindications

• Severe AI: diastolic balloon inflation $\rightarrow \uparrow$ AI \rightarrow LV distension $\rightarrow \downarrow$ CPP, \uparrow myocardial O₂

consumption

- Sepsis
- Severe vascular disease (e.g., AAA or TAA, femoral grafts or vascular dz, etc.)
- Severe LV failure
- ullet Irregular, rapid rhythms ullet makes IABP synchrony more difficult

Figure 3. Aortic Pressure Waveforms of IABP



Equipment/Components

- Placed intra-operatively, in the Cath Lab or at the bedside emergently via the femoral artery
 - Other insertion locations: ascending aortic arch, subclavian artery, axillary artery, iliac artery
- Verify placement with TEE, fluoroscopy or CXR
 - On CXR, tip should be at the anterior 2nd intercostal space and 1st lumbar vertebra
- Balloon is threaded to the descending aorta, with the tip just distal to the L subclavian artery take-off and proximal to the renal arteries
- Helium (30–50 ml) used as the inflating gas due to low density, rapid diffusion coef

Management

- Balloon inflation and deflation:
 - Synchronized to the QRS or more commonly, to an arterial waveform
 - Balloon inflation: timed to aortic dicrotic notch or immediately after the ST-T wave
 - Balloon deflation: timed to the beginning of the systolic upstroke or the start of the R wave = beginning of systole
- Markers of a correctly timed IABP:
 - Augmented diastolic BP (dBP) should be > unassisted systolic peak pressures
 - The augmented dBP is often falsely displayed as the computed sBP from a peripheral arterial line → follow MAPs in patients with IABPs instead
 - Augmented end-dBP (aka ballooned aortic end-diastolic pressure) should be *lower* than the unassisted end-dBP
 - Assisted peak sBP should be *lower* than the unassisted peak sBP

- Anticoagulation:
 - Discuss anticoagulation plan with surgeon for post-op patients (they may already be fully anticoagulated)
 - If no contraindications, start heparin gtt with goal PTT $1.5-2 \times normal$
- Positioning:
 - Keep the limb with the inserted IABP straight
- Weaning:
 - Maximum support is a 1:1 ratio of IABP-supported beats to native cardiac beats
 - Start weaning when the patient is no longer requiring maximum medical inotropic support and/or underlying issue has resolved
 - Gradually decrease the IABP ratio from 1:1 \rightarrow 1:2, 1:3, 1:4 etc., and monitor the hemodynamic response
 - To prevent thrombus formation, the IABP is not turned off in situ unless the patient is anticoagulated.

Complications

- Improperly timed inflation/deflation:
 - Early balloon inflation or late balloon deflation → ↑ LV afterload and ↓ LV ejection as LV ejects against an inflated balloon
 - Late balloon inflation $\rightarrow \downarrow$ diastolic augmentation \rightarrow sub-optimal coronary perfusion
 - Early balloon deflation → ↓ LV unloading
- Vascular injury:
 - Aortic dissection or rupture; aortic arch injury
 - Limb ischemia
 - Mesenteric ischemia
- Balloon malfunction:
 - Balloon migration: occlusion of renal or L subclavian arteries
 - Balloon entrapment:
 - Resistance to balloon catheter removal due to incomplete balloon deflation (clots in or malfunction of the gas lumen) or a kinked central catheter
 - Tx: confirm diagnosis with angiography, may require surgical removal; literature reports of successful removal after instilling and aspirating tPA, streptokinase or urokinase into the driving gas line
- Gas emboli:
 - Balloon rupture → suspect if there is blood in the driving gas line, low balloon pressure alarm, loss of diastolic augmentation → immediately stop the IABP → examine and, if needed, replace the balloon, head CT, can consider hyperbaric chamber for massive He emboli, if available
 - Air emboli from the pressure monitoring port at the tip of the balloon can cause CVAs given the port's location near the carotid arteries
- Infection
- Hemorrhage

HEART AND LUNG TRANSPLANTATION

PHILLIP CAMP, MD

HEART AND LUNG TRANSPLANT POST-OPERATIVE MANAGEMENT

General Overview, Monitoring and Key Concepts

- Multidisciplinary team management is required for most comprehensive results and best outcomes
- Specialized ICU and ICU Critical Care Nursing Team
- Highly integrated protocol-based care algorithms
- Transplant Isolation Precautions, positive pressure room, thoroughly cleaned and sanitized prior to admission, Universal precautions, 100% masks and gloves
- Comprehensive invasive and non-invasive monitoring including:
 - Modern ventilators with flow pressure curves
 - Pulmonary artery catheter
 - Arterial catheter and non-invasive blood pressure measurements
 - Urinary, gastric drainage catheters
 - Multi-lead continuous ECG monitors
 - Advanced vital sign monitors
- Continuous and/or frequent monitoring of all drains, monitors, catheters

Lung Transplant Initial Post-Operative Management

Ventilation Management

- Modified Lung Protective Strategy (for additional details see Chapter 5)
 - Keep Peak Inspiratory Pressures below 30–35 cm HO₂
 - PEEP of 10 (Dual purpose: provide acceptable pleural tissue approximation to minimize soft tissue bleeding, and to maintain lung recruitment and transcapillary gradient for improved oxygenation
 - Tidal Volumes: maintained 8–10 cc per kg of recipient ideal weight (Note: Not the same as ARDSNet management with low tidal volumes, transplanted lungs have low initial compliance due to ischemia–reperfusion injury but uniform in nature, not patchy.)
 - There are no functional bronchial arteries (as they are not anastomosed) so PA perfusion and ventilation needed for tissue oxygenation
- Fraction of Inspired oxygen concentration (FiO₂): keep as close as possible to 0.21 to maintain arterial oxygen tension (PaO₂) 80–100 mm Hg.
 - Patient transfers on 100% FiO₂
 - Check ABG frequently (Q1–4 hrs)
- Allow modest hypercapnia in setting of good oxygenation and normal pH, overly aggressive correction delays normal respiratory drive
- Extubation criteria
 - Patient is awake, alert, following commands

- Has normal spontaneous respiratory effort
- Has acceptable ventilation and oxygenation
- Has good pain control with normal respiratory effort
- Acceptable airway examination by bronchoscopy at bedside
- Patient has weaned from full support to pressure support when stable and able to maintain ventilation
- Augmentation of ventilation and oxygenation is required if:
 - Pulmonary artery pressures are elevated above >50% of systemic blood pressures, or
 - Mean PAP is >30 mm Hg with other complications, or
 - CVP is >18 mm Hg, or
 - There is evidence of right ventricular failure and or low cardiac output
 - Use nitric oxide: 0-20 PPM, or
 - Use inhaled Flolan (epoprostenol sodium; doses of 2–70 ng/kg/min using simple nebulizers)
 - Monitor the patient's Met-Hemoglobin levels
- Unique Ventilation Issues following Lung Transplantation
 - Single Lung Transplant
 - Differential response to ventilation strategy, for example, new healthy but stiff lung and retained pathology of recipient original disease (COPD, pulmonary fibrosis) must monitor to avoid overventilating or over pressurizing either lung.
 - Barotrauma, air trapping with mediastinal shift, un-anticipated dead space.
 - Use VC or PC ventilator modes, with larger (8–10 cc/kg) TV with low respiratory rate, inverse I:E ratio (COPD) or prolonged I:E (pulmonary fibrosis)
 - Possibility of lung isolation if ventilation is unmanageable without that
 - Either Single or Double Lung Transplant
 - Compromised lymphatics, fluid overload, ischemia-reperfusion injury
 - Need for regular and as needed bronchoscopy
 - Elevated PEEP

Post-Operative Bleeding: elevated risk due to common use of cardiopulmonary bypass (CPB) and systemic anticoagulation.

Considerations and Treatment Options:

- Inadequately reversed heparin
- Development of DIC due to CPB, transfusion reaction, profound inflammatory state (cystic fibrosis, pneumonia, etc.)
 - Administer antifibrinolytic agent Amicar (\varepsilon-amino caproic acid: 4–5 g loading dose iv over 60 min and continue 1 g per hr for 6–8 hrs or until bleeding subsides)
- Decreased platelets due to CPB, response to induction agent
- Fibrinolytic State secondary to retained blood and clot in chest; requires surgical evacuation
 - Administer IV antifibrolytic medication
- Poor tissue to tissue apposition in operative field
 - Increase PEEP if tolerated
- Undetected small or medium bleeding vessels
 - Medical management
 - Increase PEEP as tolerated
 - Increase tidal volume

- Assure adequate pleural drainage
- Correct incomplete replacement of coagulation factors
- Lowered core body temperature resulting in inability to establish normal clotting cascade
 - Warm patient to normothermia

Hemodynamics

- Evaluate confounding factors that may be affecting patient hemodynamic status
- Assess sequelae of other therapies or interventions
- Rule out hypotension and vasodilation related to the use of epidural analgesia
- Rule out narcotic and anesthetic-related pressure and LV depression
- Review medications and doses actually being delivered to patient (important concept as they maybe changes or incorrectly set following transfer or major movement of patient)
- Rule out on-going significant hemorrhage

Fluid Management

- Lung transplant patients differ in management from standard post-bypass cardiac patients, there is increased capillary permeability and non-functional lymphatic drainage of the graft
- Goal: keep patient slightly hypovolemic to euvolemic during fluid resuscitation Use of colloid rich solutions when able to use for secondary purpose, for example, fresh frozen plasma.
- CVP goal: 4–14 mm Hg; urine output goal: 1.5 ml/kg/hr, keep BUN:Cr ratio at 30–40; monitor daily weight
- Fluid resuscitate to functional clinical stability, for example, urine output, cardiac output, SVR, MVO2, lactate level, and base deficit
- No single perimeter should drive care management decisions, continue monitoring the patients overall clinical status ("big picture") in first 24–72 hrs post transplant

Oxygen Delivery and Transfusion Management

- Routinely maintain hematocrit above 22, with higher hematocrit goal of up to 30 based on need for improved DO₂ or associated patient co-morbidity is those conditions are better served with elevated hematocrit
- Close monitoring of post-op hemorrhage with correction and replacement
- Reverse all Heparin effects
- Rule out and treat DIC associated with underlying patient condition and CPB
- Maintain normothermia: 4°C drop in the patient's temperature will double bleeding time and will not "correct" with added blood products until the patient's temperature is normalized
- Low platelet level, or, dysfunctional platelets secondary to CPB, other platelet-related medication
 - Transfuse platelets if <50, or active bleeding
 - Consider treating for platelet dysfunction if serum creatinine is elevated and renal dysfunction is suspected
 - DDAVP (will mobilize Von Willebrand factors from storage vesicles) and will temporarily restore platelet function

Cardiac Output

- Maintain cardiac index 2.2–3.5 L/M2
- Maintain mixed venous saturation: 60%–75%

- Keep SVR: between 800 and 1,200
- Keep PVR: between 80 and 150
- Inotropic and vasoactive support
 - Epinephrine for primary cardiac support
 - Norepinephrine for Primary cardiac support with associated vasodilation
 - Milrinone for biventricular support and RV dysfunction +/- associated pulmonary hypertension
 - Vasopressin (low dose) for isolated peripheral vasodilation
 - When using Inotropes and vasoactive agents, a low dose poly-pharmacy is preferred to high-dose monotherapy with side effects
 - Frequent, serial cardiac output measurements and calculation of perfusion perimeters should be done. Measure serial MVO2. Monitor response to changes at least hourly until patients is stable

Cardiac Rhythm Management

- Sinus heart rates up to 110 BPM are typical and acceptable if stable perfusion.
- Sinus Tachycardia should not be pharmacologically blunted until other causes are ruled out and or treated, including:
 - Hypovolemia and/or hypotension
 - Inadequate pain control
 - Sequelae of other therapy or treatments
 - Generalized metabolic derangement, for example hypoxia, acidosis, etc.
- Treatment: low-dose beta blockade titrated to effect. AVOID calcium channel blockers due to effect on calcineurin inhibitor drug levels

GI and Nutrition

- Nutrition consult on admission to ICU
- Consider early, low volume ("trickle") enteric feed if no plan for extubation within 24 hrs post transplant
- Keep NPO when nearing extubation, allow sips of clears following intubation
- If short-term intubation is planned following surgery, advance diet as tolerated
- Secondary advantage is enteric feeding: many post-transplant medications can be given enterically and this can limit fluid administration

Immunosuppression

• Induction and Maintenance

- Induction initiates in OR prior to recipient blood exposure to donor endothelium
- Monitor effect of induction directly (CD3) or indirectly (Platelet count, etc.) for duration of treatment
- Induction continued for up to a week following OR, goal is functionally negate chance of significant acute rejection, and blunt risk of ischemia—reperfusion injury
- Concurrent treatment with high-dose steroids, and antihistamines
- Elevated risk for infection

Maintenance

- Begin calcineurin inhibitors once stable post operatively, delays nephrotoxicity immediately following metabolic derangement of transplant surgery
- Convert to low-dose tapered steroids following induction

• Additional immunosuppressive agents as able based on clinical stability and organ function; use oral route

Antimicrobials and Prophylaxis

- Initial Post-Operative Antimicrobial Therapy
 - Transplanted patients should be started on empiric antibacterial treatment pending airway sample culture results, unless the donor airway specimen gram stain is without neutrophils and organisms
 - For initial empiric coverage ciprofloxacin, metronidazole, and vancomycin

	Inotropic and Vasopressor Drug	Names, Clinical Indication for The (Catecholamines), and Major (Dose Rai	nge, Receptor Binding
				Receptor Binding			
Drug	Clinical Indication	Dose Range	α1	β1	β2	DA	Major Side Effects
Catecholamines				() E (S)			•
Dopamine	Shock (cardiogenic, vasodilatory) HF Symptomatic bradycardia unresponsive to atropine or pacing	2.0–20 mcg · kg ⁻¹ · min ⁻¹ (max 50 mcg · kg ⁻¹ · min ⁻¹)	+++	++++	++	++++	Severe hypertension (especially in patients taking nonselective β-blockers) Ventricular arrhythmias Cardiac ischemia Tissue ischemia/gangrene (high doses or due to tissue extravasation)
Dobutamine	Low CO (decompensated HF, cardiogenic shock, sepsis-induced myocardial dysfunction) Symptomatic bradycardia unresponsive to atropine or pacing	2.0–20 mcg · kg ⁻¹ · min ⁻¹ (max 40 mcg · kg ⁻¹ · min ⁻¹)	+	+++++	+++	N/A	Tachycardia Increased ventricular response rate in patients with atrial fibrillation Ventricular arrhythmias Cardiac ischemia Hypertension (especially nonselective β -blocker patients) Hypotension
Norepinephrine	Shock (vasodilatory, cardiogenic)	0.01–3 mcg · kg ⁻¹ · min ⁻¹	+++++	+++	++	N/A	Arrhythmias Bradycardia Peripheral (digital) ischemia Hypertension (especially nonselective β-blocker patients)
Epinephrine	Shock (cardiogenic, vasodilatory) Cardiac arrest Bronchospasm/anaphylaxis Symptomatic bradycardia or heart block unresponsive to atropine or pacing	Infusion: 0.01–0.10 mcg · kg ⁻¹ · min ⁻¹ Bolus: 1 mg IV every, 3–5 min (max 0.2 mg/kg) IM: (1:1,000): 0.1–0.5 mg (max 1 mg)	++++	++++	+++	N/A	Ventricular arrhythmias Severe hypertension resulting in cerebrovascular hemorrhage Cardiac ischemia Sudden cardiac death
Isoproterenol	Bradyarrhythmias (especially torsade des pointes) Brugada syndrome	2–10 mcg/min	0	++++	++++	- N/A	Ventricular arrhythmias Cardiac ischemia Hypertension Hypotension
Phenylephrine	Hypotension (vagally mediated, medication- induced) Increase MAP with AS and hypotension Decrease LVOT gradient in HCM	Bolus: 0.1–0.5 mg IV every 10–15 min Infusion: 0.4–9.1 mcg \cdot kg ⁻¹ \cdot min ⁻¹	+++++	0	0	N/A	Reflex bradycardia Hypertension (especially with nonselective β-blockers) Severe peripheral and visceral vasoconstriction Tissue necrosis with extravasation
PDIs							
Milrinone	Low CO (decompensated HF, after cardiotomy)	Bolus: 50 mcg/kg bolus over 10–30 min Infusion: 0.375–0.75 mcg · kg ⁻¹ · min ⁻¹ (dose adjustment necessary for renal impairment)	Hypotension Cardiac ischemia		Hypotension		
Amrinone	Low CO (refractory HF)	Bolus: 0.75 mg/kg over 2–3 min Infusion: 5–10 mcg · kg ⁻¹ · min ⁻¹		1	N/A		Arrhythmias, enhanced AV conduction (increased ventricular response rate in atrial fibrillation) Hypotension Thrombocytopenia Hepatotoxicity
Vasopressin	Shock (vasodilatory, cardiogenic) Cardiac arrest	Infusion: 0.01–0.1 U/min (common fixed dose 0.04 U/min) Bolus: 40–U IV bolus	muscle) eptors (re	scular sm		Arrhythmias Hypertension Decreased CO (at doses >0.4 U/min) Cardiac ischemia Severe peripheral vasoconstriction causing ischemia (especially skin) Splanchnic vasoconstriction
Levosimendan	Decompensated HF	Loading dose: 12–24 mcg/kg over 10 min Infusion: 0.05–0.2 mcg · kg ⁻¹ · min ⁻¹		j	N/A		Tachycardia, enhanced AV conduction Hypotension

 α_1 , indicates α -1 receptor; β_1 , β -1 receptor; β_2 , β -2 receptor; DA, dopamine receptors; 0, zero significant receptor affinity; + through +++++, minimal to maximal relative receptor affinity; N/A, not applicable; IV, intravenous; IM, intramuscular; max, maximum; AS, aortic stenosis; LVOT, LV outflow tract; HCM, hypertrophic cardiomyopathy; and AV, atrioventricular.

• Hx of multi-drug resistant bacterial or fungal colonization or pre-existing resistant gram-negative

colonization (i.e., CF or other forms of bronchiectasis), tailor antibiotics to the pre-operative known bacterial isolates (follow culture sensitivities).

- Donor culture results must be checked at 24 and 48 hrs to further direct therapy. In cases where no organism is identified and little or no purulence was observed during donor bronchoscopy, broad-spectrum empirical treatment can be discontinued after 72 hrs.
- In cases where significant purulence was observed bronchoscopically, antibacterials are often continued for 7–10 d.
- Bilateral lung transplant empirically treat with antifungals (micafungin)

• Post-Transplant Infection Prophylaxis

• PCP (Pneumocystis jiroveci)

- There was a 10%–20% incidence of PCP in the first 6 mo prior to the routine use of prophylaxis (Clin Microbiol Rev. 2004;17:770–782).
- Trimethoprim-sulfamethoxazole 1 DS tablet by mouth M/W/F or 1 SS tablet by mouth daily indefinitely. In addition to providing prophylaxis for PCP, trimethoprim-sulfamethoxazole provides prophylaxis for Listeria, Nocardia, Toxoplasmosis, and UTIs others.
- For those patients with documented allergy to sulfa, prophylaxis alternatives include desensitization to trimethoprim-sulfamethoxazole (1 ss tablet po daily), atovaquone 1,500 mg daily, dapsone 100 mg daily, and inhaled pentamidine 300 mg q2wks. Note: caution in choosing either dapsone or inhaled pentamidine as alternatives. Neither provides adequate prophylaxis for Toxoplasma IgG positive recipients. Dapsone is associated with methemoglobinemia and hemolytic anemia, which can be severe in patients with G6PD deficiency. Significant cross-reactivity between dapsone and trimethoprim-sulfamethoxazole in non-HIV infected patients.

Toxoplasmosis

• Patients with positive IgG titres against toxoplasma receive life-long prophylaxis with Bactrim one double strength tablet daily.

Viral Prophylaxis

- Among all solid organ transplant recipients, lung transplant recipients have the highest risk of CMV reactivation and disease in the absence of prophylaxis. Active CMV infection is associated with donor-positive/recipient-negative (D+/R-) CMV serostatus, rejection and other invasive infections (e.g., Aspergillus and PCP) and is also a risk factor for post-transplant lymphoproliferative disease (PTLD). The duration of CMV prophylaxis differs based on type of transplant, level of immunosuppression, and pre-transplant serologic status. D+/R- recipients are at the highest risk while D-/R- lung transplant recipients are at the lowest risk and do not require specific CMV prophylaxis.
 - Valganciclovir is our current drug of choice for CMV prophylaxis. See table below for recommendations based on donor and recipient serologic status the prophylactic valganciclovir regimens.
 - After the prescribed valganciclovir prophylaxis course is completed, CMV virus load should be monitored every month for the following 3 mo. Note that in addition to preventing CMV, valganciclovir also simultaneously prevents HSV and VZV outbreaks.
 - Patients who are D-/R- do not require valganciclovir prophylaxis for the prevention of CMV, but do require valacyclovir 500 mg po bid for 3 mo after transplant for the prevention of VZV and HSV infections.

	CMV, VZV, HSV Prophylactic Strategy		
Donor/Recipient Serologic Status	ECONO (1902 D. 1903 D. 1904 D.		
D+/R-	☐ Induction: Valganciclovir (Valcyte) 900 mg po BID × 6 mo, then ☐ Maintenance: 450 mg po BID until 12 mo post-transplant		
D+/R+	☐ Induction: Valganciclovir (Valcyte) 900 mg po BID × 6 wks ☐ Maintenance: 450 mg po BID until 6 mo post-transplant		
D-/R+	☐ Induction: Valganciclovir (Valcyte) 900 mg po BID × 6 wks ☐ Maintenance: 450 mg po BID until 6 mo post-transplant		
D−/R− □Valacyclovir (Valtrex) 500 mg po BID × 6 mo			

• Pain Management

- If no planned anticoagulation or heparin bolus associated with CPB then place epidural catheter at onset of operation.
 - Generally do not initiate infusion of epidural until hemodynamically stable and more alert, avoid confounding clinical picture with vasodilation and hypotension.
 - If planned or likely need for systemic anticoagulation, consider placement of regional infusion catheters (e.g., 'On-Q Catheter')
 - Begin infusion immediately post operatively unless hemodynamically unstable
- Systemic pain regimen
 - Used in combo with epidural or loco-regional infusion catheters
 - Opioids; NSAIDS short term only (risk of nephrotoxicity)
 - Anxiolytics, low dose as adjuvant to pain control agents

LIVER, KIDNEY, AND PANCREAS TRANSPLANTATION

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LIVER, KIDNEY, AND PANCREAS TRANSPLANTATION

Ventilation

- Aim at immediate postoperative extubation: reduced mortality, reduced costs, shorter hospital stay, higher survival rates (level 2 evidence)
- Pathophysiology: intrapleural pressure is lower in spontaneously breathing patients and linked to improved portal, venous and hepatic artery blood flow
- Note: early extubation may be difficult in patients with early graft dysfunction, retransplantation, multi-organ transplants

Fluid Management

- Intraoperative fluid restriction has beneficial influence on postoperative course
- Note: sodium/water retention due to liver cirrhosis, intraoperative capillary leak syndrome with "third spacing" and steroid application lead to fluid overload
- Risks: cerebral edema, pulmonary complications, graft swelling and portal hypertension
- Thus, try to keep the patient "dry" (aim at CVP around 5, but not higher than 10 mm Hg)
- If necessary, replace intravascular fluids with colloids rather than Ringer's lactate (RL) as lactate is usually elevated
- Depending on hemodynamic stability, CVP, urine output, hematocrit and other hemodynamic factors, maintaining an appropriate negative fluid balance during the first 3 d may reduce the risk of early pulmonary complications and prolonged ventilation (level 2C evidence)
- However, the fluid balance needs to be estimated individually and requires frequent re-assessments
- Hemodynamic instability may also be caused by myocardial dysfunction during the reperfusion phase and may persist postoperatively
- Assess for an appropriate preload and afterload and use inotropes (dobutamine, dopamine) if necessary

Nutrition

- Preoperative hypocaloric malnutrition is common and TPN should be commenced 24 hrs postsurgery
- Enteral nutrition (EN) should be started as soon as possible (i.e., on POD 3) for maintenance of mucosal integrity (level 2C evidence)
- A jejunal double lumen tube may be placed in ventilated patients
- Gastric reflux needs to be assessed to calculate volume of EN

Immediate Postoperative Lab Work

• Potassium – hyperkalemia due to preservation fluid entering into the circulation and a temperature

impaired sodium–potassium transporter. Calcium – transfusion of citrate-containing blood products may decrease Ca and Mg levels

• Magnesium, phosphorus – keep Mg and PO₄ levels high to avoid muscle weakness and seizure.

Note: CNI and hypomagnesemia decrease the seizure threshold

- Lactate lactate levels should normalize quickly after transplantation. Persisting elevated lactate levels may suggest hypoperfusion or poor graft function
- Every 6 hrs: hematocrit, INR, transaminases

Graft Function and Serum Transaminases

- Transaminases usually peak by day 2–3 (usually up to 2,000 U/l) and decrease rapidly thereafter
- Often, normal transaminase levels or slightly elevated levels are reached within a week, depending on preservation injury and organ quality (donor age, degree of steatosis, cold ischemia time and others)
- Extremely high serum transaminases, a second peak or failure to normalize should be examined immediately to rule out early postoperative complications (see below)
- Adequate graft function is linked to normal blood glucose, production of dark bile, improving coagulation, hemodynamic stability and metabolism of anesthetic agents and steadily improving neurologic status

Immunosuppression

Immunosuppressive protocols vary with center preference and patients may be included in clinical studies.

Induction Therapy

Induction agents are not commonly used in liver transplantation, approximately 25%–30% of liver transplant recipients receive induction therapy.

Basiliximab (Simulect)

- Humanized IL-2 receptor antibody directed against the CD25 molecule on T-cells
- Inhibits activation and proliferation of T-cells
- Dose: 20 mg IV, given on days 0 and 4, causes IL-2 saturation for about 42 d
- Few side effects (hypersensitivity)

Antithymocyte Globulin (ATG)

- Polyclonal, purified IgG fraction directed against human lymphocytes
- Depletion of circulating T-cells mainly through complement-dependent lysis or activation-induced cell death (AICD)
- Thymoglobulin (1.5 mg/kg/d)/ATG (Fresenius) single dose (8 mg/kg)
- Side effects: infusion reaction, anaphylaxis, serum sickness (rash, joint, and muscle aches), thrombocytopenia/leukopenia, antibody formation, increased risk of malignancies

Alemtuzumab (Campath 1H)

- Humanized monoclonal CD52-specific IgG1
- Rapidly depletes not only T-cells but also NK-cells, B-cells
- Dose can vary; usually 30 mg iv on days 0 and 1
- Common side effects with the first dose (infusion reaction): fever, chills, rigors, nausea, urticaria, but also severe hypotension and bronchospasm

- Administer antihistamine (i.e., chlorpheniramine 30 mg iv> or diphenhydramine 30 mg iv) simultaneously to prevent infusion reaction
- Note: severe pancytopenia

Maintenance Immunosuppression

- Adapted to immunologic risk profile; doses are higher in the immediate posttransplant period and reduced thereafter
- Maintenance immunosuppression (IS) usually consists of tacrolimus, which has largely replaced cyclosporine, and steroids, often combined with MMF, which has mostly replaced azathioprine
- Steroid withdrawal or minimization is becoming increasingly common

Tacrolimus (Prograf)

- Binds to FK-binding protein and inhibits calcineurin (calcineurin inhibitor: CNI), which ultimately inhibits IL-2 production and production of pro-inflammatory cytokines, thus inhibiting T-cell proliferation
- Start of treatment with dosing of 0.15 mg po bid or 0.01–0.05 mg/kg/24 hr iv) and initial target trough levels (i.e., 8–12 ng/ml) with local variations in dosing
- Interference with Cytochrome P450 system causes various drug interactions which may affect trough levels
- Side effects include nephrotoxicity, neurotoxicity, hypertension, hyperglycemia, hyperkalemia, hypomagnesemia, posttransplant lymphoproliferative disorder (PTLD)

Mycophenolate Mofetil (Cellcept) and Mycophenolate Sodium (Myfortic)

- Inhibition of inosine monophosphate dehydrogenase and production of quanosine nucleotides prevents T-cell and B-cell proliferation
- 500 mg mycophenolate mofetil (MMF) equal 360 mg mycophenolate sodium
- Mycophenolate sodium is an enteric-coated formulation designed to minimize the gastrointestinal side effects
- Graft dysfunction can impair its conjugation and thus cause higher serum levels
- The use of MMF varies with local transplant protocols
- Dosing: usually MMF 1 g po bid is given, depending on absolute neutrophil counts (ANC) or WBC counts
- Side effects are myelosuppression, gastrointestinal symptoms (nausea, vomiting, diarrhea, abdominal pain)

Corticosteroids

- Inhibit formation of arachidonic acid through binding to intracellular receptors
- Broad effects on cellular response although little specific
- Sparing of humoral response
- Side effects include osteopenia, hypertension, hyperlipidemia, hirsutism, ulcer disease, glucose intolerance, cataracts, psychosis, weight gain, and many more
- Usually a first high dose (i.e., 500 mg Prednisolone iv) is administered intraoperatively with subsequent tapering of steroids

Thromboprophylaxis

- Postoperative thrombocytopenia and coagulopathy usually preclude thromboprophylaxis in the first days after transplantation
- Use unfractionated heparin (i.e., 5,000 units bid sc or iv) when starting thromboprophylaxis and

switch to low molecular heparin upon discharge from the ICU

Antimicrobial Prophylaxis

Antifungal Prophylaxis and Therapy

- Fungal infections usually occur within the first weeks after transplantation
- Patients at increased risk: those requiring reoperations or renal replacement therapy, retransplanted patients
- Avoid extensive use of broad-spectrum antibiotics
- Fluconazole impairs the Cytochrome p450 metabolism of tacrolimus and will increase tacrolimus trough levels substantially.
- Distinguish between colonization (often in bronchial washings, sputum, nasal secretions) and infection

Prophylaxis

- Prophylaxis with fluconazole is widely used but may increase the risk of non-Candida infections. Recent studies suggest that antifungal prophylaxis should be limited to high-risk patients (level 1A evidence)
- Prophylaxis with fluconazole 400 mg per oral should be continued for 4–6 wks
- Selective digestive decontamination (SDD): not evidence based and increases the risk of infection and is thus not recommended (level 1A evidence)

Treatment

- Positive culture for Candida albicans fluconazole 400 mg once daily per oral
- Positive cultures for non-Candida species Caspofungin iv 70 mg once as a loading dose followed by Caspofungin 50 mg iv once daily on the following days

Antibiotic Prophylaxis

- Broad-spectrum antibiotic prophylaxis consisting of meropenem, piperacillin/tazobactam or ampicillin and gentamicin are commonly used for 3–5 d posttransplant or until all lines and catheters are removed
- Note: antibiotic prophylaxis should be kept to a minimum, i.e., 24–48 hrs maximum transplantation due to the risk of increasing drug resistance (gram-negative bacteria!)

TB Prophylaxis

• Patients at risk (history of TB, born in Asia/Africa) may receive isoniazid 200 mg per oral once daily + pyridoxine 10 mg per oral once daily for the first year after transplantation

PCP Prophylaxis

• PCP prophylaxis (i.e., co-trimoxazole 480 mg per oral once daily) is used in the early posttransplant period for 3–6 mos

CMV: Prophylaxis and Therapy

- CMV infection occurs primarily in the first 3 posttransplant months when immunosuppression is most intense
- It can cause graft dysfunction and is associated with the development of opportunistic infections, acute rejection and vanishing bile duct syndrome
- CMV infection: isolation of CMV from blood or tissue
- CMV disease: fever >38°C, neutropenia or thrombocytopenia and CMV viremia
- CMV disease often affects the GI tract (esophagitis, gastritis, colitis, enteritis) and less often other organs (lungs, heart)

• Prophylaxis is usually preferred over pre-emptive therapy but approach varies

CMV Infection of the Liver Graft

- Graft dysfunction (i.e., elevation of serum transaminases) and quantitative CMV-RNA detection in blood
- Confirmation by liver biopsy
- Clinical, mononucleosis-like symptoms may include leucopenia, fever, night sweats, arthralgia
- Associated with long-term biliary complications

Prophylaxis

- Recommended for CMV (D+/R-) seropositive donor/seronegative recipients receive constellations
- Note: often applied in all recipients except D-/R- recipients
- Oral ganciclovir 3 g/d for 3 mos has mostly been replaced by valganciclovir (450 mg 2 times daily, if renal function is normal) or Valacyclovir (1 g 3 times daily)
- Disadvantage of prophylaxis: no prevention of primary disease, prolonged drug exposure, increased risk of drug resistance and delayed or late onset CMV infection

Pre-emptive Treatment

- Therapy is started upon positive CMV findings
- Intention: detection of CMV reactivation prior to clinical symptoms
- Requires frequent monitoring
- Note: patients may develop CMV disease prior to the detection of CMV-RNA
- Recommended for medium- or low-risk patients (R+) recipients
- Mostly valganciclovir is used (900 mg 2 times daily, if renal function is normal), iv ganciclovir 5 mg/kg 2 times daily is equivalent (level 1A evidence)

Treatment of CMV Infection

- I.V. ganciclovir 5 mg/kg 2 times daily depending on renal function (level 1A evidence) for at least 2 wks
- The duration of treatment should be individualized, it may be continued until 2 × negative CMV-DNA testing in peripheral blood
- If low risk for recurrence: consider prophylactic treatment for additional 2 wks
- If high risk for recurrence: consider prophylactic treatment for 3 mos
- Treatment may be switched to valganciclovir 450 mg 2 times daily at a later time point if patient is well (VICTOR study group: equivalent to ganciclovir), however valganciclovir is not licensed for CMV treatment in organ transplant recipients = off label use
- Monitor CMV-PCR at least twice weekly for changes
- In case of severe infection: add CMV-IgG (2 ml/kg) (level 2B evidence), yet benefit is unclear
- Decrease of baseline immunosuppression (i.e., MMF)
- Also consider treatment of asymptomatic patients with high viral load (>10,000 copies) as it is correlated with risk of CMV disease

Hepatitis B

- Pretransplant HBV therapy can prevent posttransplant recurrence
- Recurrent hepatitis can be life threatening if undetected
- Check for anti-Hbs titers and HBV DNA (PCR, blood)

Commonly Used HBV Prophylaxis Regimens

• HBV-Ig alone until anti-Hbs titer >500 IU/l (however high costs, recurrence due to HBV mutants)

- HBV-Ig and lamivudine (superior to any monotherapy, lower costs, lower recurrence rate) (level 2A evidence), doses and duration of treatment vary between centers
- Of note: up to one-third of patients with posttransplant HBV recurrence have developed mutant forms (YMDD) during pretransplant lamivudine therapy
- Prophylaxis of patients with mutant HBV forms should include drugs with better resistance profile (tenofovir or adefovir)

Treatment of Recurrent HBV Infection

- As a consequence of posttransplant immunosuppression, HBV recurrence may progress rapidly if prophylactic therapy fails
- Due to high lamivudine resistance rates, adefovir (10 mg daily depending on renal function) w/wo HBV-Ig may be the first choice of treatment (level 2B evidence)

Hepatitis C

- HCV associated liver cirrhosis is the most common indication for OLT
- Posttransplant recurrence is almost certain, resulting in 10–20-fold increase in HCV RNA levels after the first week, 20%–30% cirrhosis after 5 yrs and a lower long-term outcome compared to other indications for OLT
- Currently, there are no convincing data available demonstrating a beneficial impact of any immunosuppressive drug (Tac, CyA, MMF, steroids) over another in regard to HCV recurrence
- ATG for induction therapy may be used with caution, while IL-2R antagonists do not seem to influence the course of HCV recurrence

HCV Prophylaxis After Orthotopic Liver Transplant (OLT)

- Few studies are available showing mixed results regarding the efficacy of PEG-interferon alfa-2a prophylaxis +/- Ribavirin with sustained viral response (SVR) rates between 0% and 33%
- Adverse effects (mostly anemia) are common (up to 50%)
- While PEG-IFN + Ribavirin, if tolerated, may have beneficial effects on histologic changes and HCV-RNA levels, standard pre-emptive therapy cannot be recommended

Treatment of Recurrent HCV Infection

- Generally, response rates to treatment are low due to the combined bone marrow suppressive effects of interferon and immunosuppressants and side-effects of Ribavirin frequently requiring dose reduction or discontinuation of treatment
- Consider decrease of immunosuppression in case of severe HCV-infection (adjust tacrolimus levels depending on time after transplantation and individual immunologic risk) and avoid steroid bolus treatment for mild acute rejection if possible (increase/add MMF)
- Early virologic response (EVR) defined as negative HCV-RNA or 2-log decrease of HCV-RNA is a positive predictor of SVR
- Standard therapy: PEG-interferon (1.5 mcg/kg/wk) + Ribavirin (400 mg–1,200 mg/d) offer good results (SVR > 30% on average) with an EVR > 50%
- However, interferon intervention is associated with a higher risk of acute and chronic rejection
- Side effects include myelosuppression, hemolysis, rejection, infection and depression

Differential Diagnosis

- The differentiation between AR and HCV infection in liver biopsies can be difficult because of overlapping features (portal inflammation, ductal damage, endothelialitis)
- An interdisciplinary approach is recommended for the assessment of unclear biopsy findings;

clinical features need to be considered

• Annual liver biopsy should be performed to evaluate the disease progression

Bacterial Infection

- Sepsis is a common cause of early patient death
- Frequent infections are: pneumonia, catheter associated sepsis, intra-abdominal abscess (bile leakage?) cholangitis, SBP, wound or urinary tract infections
- When fever or rising WBC/CRP:
 - Chest X-ray, Doppler ultrasound, cultures of urine, blood, bile
 - Check lines: change lines if other causes of fever are ruled out

Doppler Ultrasound

An immediate postoperative and thereafter daily ultrasound should be conducted to assessment:

- fluid collections hematoma, intra-abdominal abscess
- liver perfusion and liver parenchyma preservation injury, subcapsular hematoma, abscess
- pleural effusion

X-rays

- Daily chest X-rays should be performed for monitoring of fluid balance and pleural effusions
- T-tube cholangiogram on day 7 for detection of anastomotic stricture or leakage

Drains, Lines and Catheters

- Should be removed as early as possible
- Are sources of early infections. In high-risk patients, antibiotic prophylaxis (i.e., amoxicillin) may be maintained until all lines and catheters are removed
- T-tubes are a valuable indicator of bile production and quality. Following a T-tube cholangingram, the tube should be closed to allow for physiologic bile flow and remain in place for 2–6 wks
- Note: a closed T-tube restores the enterohepatic circulation and can lead to increased drug levels of MMF and CNI
- Drains and Catheters should not be removed without consulting transplant surgery

Postoperative Complications: Rising Liver Function Tests Early Graft Dysfunction

- Steep increase in transaminases, bilirubin, and non-resolving coagulopathy
- Elevated NH₃ is associated with poor neurologic status therefore avoid benzodiazepines, assess neurologic status (extubation!)
- preservation injury usually goes along with improving neurologic status and improving prothrombin time while primary non-function is usually associated with worsening mental status and decreasing coagulation profile

Primary Non Function

- Related to: prolonged cold ischemia time, severe hepatic steatosis, profoundly elevated donor sodium levels (>165 mEq/l)
- 1%–5% of liver grafts fail

- Symptoms: highly elevated serum transaminases, severe acidosis despite patent vessels, severe coagulopathy, poor bile production, hemodynamic instability
- Treatment is symptomatic, prostaglandin E₁IV may have beneficial effects
- Only causative treatment is immediate retransplantation

Neurologic Complications

- Usually occur in the first 2 wks posttransplant
- Presentation is most commonly with altered mental status, acute delirium, seizures, fever, visual abnormalities, tremors, and coma
- Most common causes include sleep deprivation, high-dose steroid therapy, electrolyte abnormalities, use of calcineurin inhibitors, and systemic infections
- Rarely central pontine myelinolysis and viral encephalitis may occur
- Head CT scans and Magnetic Resonance Imaging may be required for diagnosis
- Treatment: immunosuppressive and steroid doses may need to be adjusted. Prognosis is excellent in patients with seizures and recovery from coma is seen within days after transplantation. The prognosis for central pontine myelinolysis is poor

Vascular Complications *Hepatic Artery Thrombosis*

- Restrictive platelet transfusion (threshold 20,000) and avoidance of graft swelling (fluid restriction) increase hepatic artery flow
- Often occurs in small caliber anastomosis
- 3%–5% incidence in adults, overall mortality is 33%
- Clinical symptoms vary widely from asymptomatic patients with almost normal liver tests to markedly rising transaminases, clinical deterioration, fever and increasing WBC's
- A rise in transaminases should lead to an immediate Doppler ultrasound and if findings are suspicious, a CT angiogram should be performed
- If detected early, thrombectomy and/or correction of arterial anastomosis may restore blood flow. Following this procedure anti-coagulation (unfractionated heparin, aPTT > 45 sec) is mandatory
- If thrombosis persists: high risk of hepatic abscesses, risk of necrosis of intrahepatic and extrahepatic biliary tree (Sepsis!), long-term consequence: ischemic biliary lesions with non-anastomotic strictures
- **Note:** consider early retransplantation since ultimately 53% of patients with hepatic artery thrombosis require retransplantation

Portal Vein Stenosis or Thrombosis

- Incidence about 2%, representing a severe complication
- Patients at risk are those with previous portal vein thrombosis or previous portacaval surgery and patients with portal vein reconstruction when an interposition graft is utilized
- Rapid clinical deterioration may occur and is associated with: severe graft dysfunction, hemodynamic instability and kidney failure
- As with hepatic artery complications, an early diagnosis allows successful surgical intervention, but often retransplantation is required

Bile Duct Complications

- "Achilles Heel" of the procedure, up to 20% of all patients develop biliary complications, severity of clinical consequences vary
 - Bile leakage:
 - Usually early after transplantation
 - Sites at risk: bile duct anastomosis/choledochojejunostomy, graft cystic duct stump
 - Clinical symptoms can vary widely, therefore fever and/or abdominal pain should raise attention towards bile duct complications
 - Check surgical drains for bile and test for bilirubin levels in all surgical drains
 - Ultrasound/CT scan: fluid collection? A biloma needs to be drained
 - Often endoscopical treatment (ERC with placement of a biliary stent) is sufficient
 - If endoscopic treatment is not sufficient (i.e., due to bile duct necrosis): a choledochojejunostomy might be required
 - Biliary strictures:
 - Early or late after transplantation
 - Bile duct strictures are not always associated with intrahepatic cholestasis and biliary dilation, hence: a rise of bilirubin, gGT and AP should have a low threshold for a MRCP
 - Treatment of choice: balloon cholangioplasty and/or biliary stent
 - In some cases, especially when late anastomotic strictures occur, surgical revision of bile duct anastomosis or choledochojejunostomy is required
 - Patients with multiple intrahepatic strictures are often caused by peritransplant ischemia (IBL or ITBL) and frequently require retransplantation

Bleeding

- 5%–10% of patients will require reoperation for continued bleeding
- Attributable to lack of clotting factors, fibrinolysis, thrombopenia
- Be suspicious for bleeding in case of postoperative hypotension or oliguria
- Assess drains and hematocrit/hemoglobin frequently after transplantation
- Avoid low molecular heparin in the early period after transplantation

Acute Cellular Rejection

- 15%–25% of liver transplant recipients experience cell mediated rejection yet it rarely leads to graft loss
- often occurs within first month posttransplant
- clinical symptoms may be fever, graft tenderness and dysfunction, jaundice, but rejection often presents as asymptomatic elevation of transaminases
- histologic signs are portal inflammation with lymphocyte infiltration, subendothelial infiltrates in portal veins and bile duct inflammation
- commonly, treatment consists of steroid pulse therapy and increase of baseline immunosuppression
- mild rejection may occasionally be treated with increasing of maintenance immunosuppression
- any treatment must consider the severity of rejection, the original disease and the particular medical history of the patient

Hepatitis C Infection and Acute Rejection

• Requires special consideration as treatment with high-dose steroids or T-cell depleting therapy may cause a flare up of HCV progression

- Diagnosis is also difficult as the biopsy features of HCV infection and acute rejection may mimic each other
- Many centers will initially defer treatment if diagnosis of rejection is unclear or if only mild rejection is suspected
- If repeat biopsy confirms rejection treat by increasing the dose of calcineurin inhibitor and/or adding an adjuvant agent such as MMF

Acute Humoral Rejection

- very uncommon after liver transplantation
- mediated by preformed antibodies against ABO antigens, HLA antigens or endothelial antigens
- liver biopsies show complement fixation and fixation of antibodies, necrosis, neutrophil infiltrates
- treatment includes B-cell depletion using rituximab (anti-CD20 mab) and/or plasmapheresis

Primary Non-function (PNF)

- reported incidence about 5% with a variation between 1% and 24%, accounting for about one-third of early graft losses after liver transplantation
- risk factors may include increased donor age (reduced repair capacities), graft macrosteatosis (reduced liver flow due to narrowing of the sinusoidal space), long cold ischemia time, small-forsize grafts (i.e., in pediatric transplantation) and other factors (endotoxins from the gut or hepatotoxic agents)
- Surgical technical (i.e., hepatic artery or portal vein thrombosis), immunologic, infectious
- in most cases a clear pathogenesis cannot be discerned
- lab signs: steep rise of transaminases, constant increase of bilirubin, severe coagulopathy, lactate acidosis and hypoglycemia
- clinical picture: signs of liver failure such as lack of bile production, hepatic encephalopathy and brain edema, renal failure and instable hemodynamics
- hyperdynamic circulation associated not only with hypotension, metabolic acidosis, organ hypoperfusion but also arterial hypertension may be present and may mimic signs of sepsis
- the treatment is symptomatic:
 - Rule out surgical technical causes (Doppler, Angio CT, MR)
 - Detoxification through albumin dialysis (MARS system) which removes albumin bound and water-soluble toxins leads to improvement of encephalopathy and renal function
 - Hypoglycemia: constant glucose substitution
 - Metabolic acidosis (sodium bicarbonate 50–180 mEq diluted in 11 D5W, depending on severity of acidosis)
 - Bleeding: check coagulation parameters and thromboelastography, administer fresh frozen plasma and, if necessary, replace factors VII, IX, X through factor concentrates
 - Intracranial edema/hypertension: place patient in head up position, check for need of intracranial pressure monitoring, use 20% mannitol 0.25 gm/kg infusion, note: hyperosmolality
 - Encephalopathy: avoid neomycin, administer lactulose via nasogastric tube every 6–8 hrs), intubated patients require a CCT scan and EEG follow-up
 - Renal failure: continuous veno-venous hemodiafiltration (CVVHDF)
 - Hypotension: initially challenge with colloids and replace red blood cells, then use inotropes such as dopamine followed by noradrenaline if necessary
 - Sepsis treatment

- Ventilation: keep PEEP as low as possible (5 cm H_{2O}) (negative effects on cerebral edema and hepatic perfusion)
- Treat hypoalbuminemia (20% albumin, fresh frozen plasma)
- GI bleeding prophylaxis (iv high-dose PPI, 20–40 mg once daily)
- Nutrition: nasogastric nutrition using liver-specific formulas, avoid iv nutrition
- Discontinue all potentially hepatotoxic agents
- Randomized, controlled trials did not show beneficial effects of prostaglandin E1 in the treatment of PNF
- Only definite treatment: retransplantation
- high risk of mortality without retransplantation as a consequence of severe brain damage, sepsis, and multi-organ failure

Management of Renal Transplant Patients

- Kidney transplantation is the treatment of choice for patients with end stage renal disease (ESRD)
- Compared to dialysis it is associated with improved outcomes, better patient survival and improved quality of life. Kidney transplantation is more cost effective
- Current 1 yr graft survival rates are 96% for living donors and 90% for deceased donors
- In 2007, 17,513 kidney transplants were performed in the Unites States
- For transplant recipients who survive the first year with a functioning transplant, 50% of deceased and living donor transplants are projected to be alive with a functioning transplant at 13 and 23 yrs, respectively. Cardiovascular disease is the leading cause of death, accounting for 30% of deaths in patients who died with a functioning transplant
- Infectious complications (21%) and malignancies (9%) are the other main causes of mortality with a functioning allograft
- Transplant complications requiring readmission and hospitalization occur at a rate of 41 admissions per 100 patient years, in the first year after transplantation
- The incidence of admission to the ICU varies from 1%–25%
- Transplant patients who are admitted to the ICU either in the immediate postoperative period or later have a higher mortality than the general ICU patient
- The majority of renal transplant patients do not require ICU management and are transferred to the floor after a few hours in the Post-anesthesia Care Unit
- The primary reasons for ICU admission are surgical and medical complications

Postoperative Fluid Management

- Maintain intravascular volume at normal or slightly increased levels with a central venous pressure (CVP) between 10–14 cm of water
- Replace urine output with half-normal saline on a milliliter per milliliter basis
- Half-normal saline is chosen because the sodium concentration of the urine from a newly transplanted kidney is 60–80 mEq/l
- If the patient is noted to be hypovolemic, isotonic saline boluses are given in 500 ml increments
- Hemodynamic and clinical evidence of hypervolemia is managed by the use of diuretics, most commonly furosemide
- Dialysis may be required for fluid overload not responsive to diuretics and for hyperkalemia and

delayed graft function

Surgical Complications

- Hemorrhage is uncommon after kidney transplantation
- Intraoperative catastrophic bleeding from the vascular anastomosis (arterial and venous) may require continued resuscitation in the ICU even after primary control was obtained in the operating room
- Ongoing bleeding may be from unligated vessels in the hilum of the transplanted kidney or from the retroperitoneal surface
- Aggressive resuscitation with blood and blood products is usually required to restore hemodynamic stability
- The incidence of graft thrombosis is low (<1%) but it almost always results in allograft nephrectomy with only few exceptions

Medical Complications

- Cardiac: careful pretransplant evaluation and selection, in addition to appropriate and timely management of cardiovascular risk factors before transplantation is essential in reducing risks for posttransplant cardiac events
- The incidence of cardiovascular disease in transplant recipients is nearly 2 times that of the general population (Data from United States Renal Data System)
- Hypertension and diabetes contribute significantly to the elevated cardiac risk
- Attention to fluid and electrolyte management is vital
- Delayed graft function may require fluid restriction and dialysis to correct volume status and electrolyte imbalances
- Myocardial infarction and pericarditis are both uncommon but need urgent management
- Pulmonary:
 - Pulmonary complications may occur as a result of fluid overload, infections or complications of immunosuppressive therapy
 - Fluid restriction and diuresis should be instituted
 - Pneumonia is common and the diagnosis should be pursued aggressively and the appropriate treatment instituted
 - Rarely, induction immunosuppressive agents such as alemtuzumab and thymoglobulin can cause flash pulmonary edema and allergic responses with hemodynamic instability
 - Respiratory failure and the need for mechanical ventilation is a predictive factor for increased mortality
- Infections:
 - Infectious complications are one of the most frequent reasons for ICU admission in kidney transplant recipients
 - The risk of infection is determined by the severity of the offending organism as well as the burden of immunosuppression
 - Early diagnosis and aggressive treatment is imperative
 - Immunosuppressive agents may require a reduction in their doses and in cases with life threatening infections, complete withdrawal of immunosuppression may be necessary
 - The ICU team should work closely and communicate all decisions regarding the care of severely ill transplant patients with the transplant team, especially in regards to dosing of

immunosuppressive agents, and monitoring of drug levels

- Neurologic:
 - Cerebrovascular accidents and seizures are the commonest neurologic complications
 - They may be a consequence of a preexisting medical condition or a complication of surgery
 - Calcineurin inhibitors (CNIs) used as maintenance immunosuppressive agents may cause neurologic side effects such as headache, tremors, seizures, and sometimes a rare demyelinating neuropathy
 - Perioperative high-dose steroid use may induce psychosis and steroids should be weaned as soon as possible
- Gastrointestinal:
 - Both upper and lower gastrointestinal complications may occur, such as peptic ulcer disease and perforation of the colon
 - The routine use of H₂ blockers has diminished the incidence of upper gastrointestinal bleeding and perforation following transplantation
 - A high index of suspicion should be entertained for bowel perforation as immunosuppressive medication and steroids may mask clinical findings

Immunosuppression

- Immunosuppressive treatment begins with the induction phase, perioperatively and immediately after transplantation
- The goal of induction therapy is to prevent acute rejection during the early posttransplantation period by providing a high degree of immunosuppression at the time of transplantation. Induction treatment allows delaying the application of calcineurin inhibitors, thus reducing nephrotoxic side effects in the early period after transplantation
- All of the induction immunosuppressive agents currently used are biologic agents and are either monoclonal (daclizumab, basiliximab, alemtuzumab) or polyclonal (antithymocyte globulin [equine] or antithymocyte globulin [rabbit]) antibodies
- Currently, approximately 70% of renal transplant recipients receive some form of induction therapy
- The most commonly used induction agent is thymoglobulin

Maintenance Immunosuppressive Agents

- Maintenance immunosuppressive therapy is administered to renal transplant recipients to prevent acute rejections
- the level of chronic immunosuppression is slowly decreased over time to help reducing the overall risk of infection and malignancy
- The major immunosuppressive agents that are currently being used in various combination regimens are calcineurin inhibitors (tacrolimus, cyclosporine), MMF, mycophenolate sodium (myfortic), corticosteroids (primarily oral prednisone), azathioprine, and rapamycin (sirolimus)
- Triple immunosuppression consisting of tacrolimus, MMF and prednisone is the most widely used maintenance immunosuppressive regimen
- Tacrolimus levels must be carefully monitored. Initially, levels can be kept in the range of 10–15 ng/ml and reduced after 3 mos (5–10 ng/ml) to reduce the risk of nephrotoxicity
- **Drug interactions** several commonly used drugs interfere with the metabolism of calcineurin inhibitors (tacrolimus, cyclosporine) and therefore may cause either overdosing with deterioration of renal function or underdosing with an increased incidence of rejection

- Drugs that increase the level of calcineurin inhibitors are
 - Calcium channel blockers verapamil, diltiazem, nicardipine, and amlodipine
 - Antifungal agents ketoconazole and fluconazole
 - Antibiotics erythromycin and clarithromycin
 - Protease inhibitors saquinavir, indinavir, nelfinavir
 - Grapefruit juice
- Common medications that decrease the level of calcineurin inhibitors (by inducing hepatic metabolism) include:
 - Anticonvulsants barbiturates, phenytoin, and carbamazepine
 - Antituberculous agents isoniazid and rifampin
 - Antibiotics imipenem, cephalosporins, ciprofloxacin, nafcillin
 - Herbal preparations, Saint John's wart
- In addition, nephrotoxic agents such as such as non-steroidal anti-inflammatory drugs, aminoglycosides, and amphotericin B may worsen the renal toxicity of calcineurin inhibitors
- In conclusion, a small (\sim 5%) percentage of renal transplant patients need ICU admission
- The most common reasons are infections and postsurgical complications
- ICU admission is associated with higher mortality with mean arterial pressure on admission and the need for mechanical ventilation predictive of a poor prognosis
- A multi-disciplinary approach with involvement of the ICU and the transplant teams is required to ensure favorable outcomes and reduce mortality and morbidity

Management of Pancreas Transplant Patients

- Patient survival rates at 1 yr were >95% in each recipient category, with 1 yr primary pancreas graft survival rates of 85% for simultaneous pancreas and kidney transplants (SPK) and 78% for pancreas after kidney transplants (PAK)
- Purpose: restore endogenous insulin production and render the patient insulin-free
- A successful pancreas transplant improves quality of life, eliminates acute complications (hypoglycemia/ketoacidosis), and enhances life expectancy
- Pancreas transplant recipient fall under three categories
 - SPK, usually from the same deceased donor in a patient who has both ESRD and insulindependent diabetes
 - PAK, in a patient with nephropathy corrected by a kidney transplant and is now waitlisted for a pancreas transplant
 - Pancreas transplant alone (PTA), in a patient with normal kidney function. PTA should only be considered a therapy in patients who exhibit: (a) history of frequent, acute, and severe metabolic complications requiring medical attention; (b) clinical and emotional problems with exogenous insulin therapy that are so severe as to be incapacitating; and (c) consistent failure of insulinmanagement to prevent acute complications

The Pancreas Donor

- Donor selection and organ procurement are vital to success
- The ideal pancreas donor: age 15-40 yrs, weight 30-80 kg; death from trauma
- Factors associated with an increased risk of graft thrombosis are (a) donor age >40 yrs, (b)

- cardiovascular or CVA as a cause of brain death, and (c) pancreas preservation time >24 hrs
- Visual organ inspection and palpation during procurement is critical to success
- Other risk factors: prolonged length of hospital stay, multiple blood transfusions, BMI > 30, need for multiple vasopressor agents, alcohol abuse, and prior splenectomy

Surgical Technique

- Lower midline incision, intraperitoneal approach; in SPK: kidney is anastomosed to the left iliac vessels and the pancreas is placed on the right side with the portal vein draining into the right external or common iliac vein (systemic venous drainage)
- The exocrine secretion of the pancreas can be drained with an enteric (ED) or a bladder (BD) anastomosis
- Bladder drainage (popular in the 80s- early 90s: safe, allows measurement of urinary amylase to monitor graft function, and anastomotic complications are easier to manage but associated with significant metabolic and urological complications due to obligatory fluid and electrolyte losses
- Enteric drainage is more physiologic and avoids metabolic acidosis and urinary complications but technical failure rates are slightly increased due to anastomotic leaks
- Currently, 70%–80% of all transplants are performed with primary enteric drainage. According to IPTR data, patient survival rates are similar for BD and ED cases in all the three categories, ranging from 94%–98% at 1 yr

Postoperative Management

- Patients are transferred to the ICU
- Extubated in the OR if operation was uneventful; remain intubated if concerns about volume status or hemodynamic stability
- Patients are kept NPO with a nasogastric tube in place
- Monitor fluid and volume status
- Intravenous antibiotics are administered for 5 d with coverage to include bacterial, viral, and fungal infections
- Accuchecks are performed q1h to maintain blood glucose below 150 mg/dl
- Insulin drip can be utilized if blood sugar is > 150 mg/dl as uncorrected hyperglycemia may be deleterious to the pancreatic beta cells of the allograft
- Avoid dextrose-containing solutions as this may cause elevation in blood glucose and make it more difficult to assess endocrine function of the allograft
- Graft function is monitored by a combination of lab studies and imaging methods which include serum creatinine, urinary amylase (in bladder drained recipients), serum amylase and lipase, and C peptide levels
- Persistent elevation in blood glucose may indicate graft thrombosis
- Imaging studies: duplex ultrasound of the allograft or a nuclear medicine scan

Surgical Complications

- Surgical complications: seen more commonly with pancreas vs. kidney transplantation; technical failure rate of 6%–10%
- The majority of complications are related to graft thrombosis, anastomotic leaks after bladder or enteric anastomosis, pancreatitis, and infections
- Early thrombosis, within the first 24–48 hrs, usually due to venous thrombosis of the portal vein is

the most common cause of non-immunologic graft loss in the first year. Pancreatitis occurs in 10%–20% of cases and is caused by ischemic damage to the organ during preservation and reperfusion

• Management: conservative, includes the somatostatin analog octreotide

Immunosuppression for Pancreas Transplantation

- The risk of pancreas allograft rejection > kidney, likely due to the greater immunogenicity of the pancreatico-duodenal graft
- Immunosuppression for pancreas transplantation has evolved over the last decade Induction therapy is most frequently applied
- The most common agents used are thymoglobulin (44%), alemtuzumab (19%), basiliximab, or daclizumab (18%)
- The majority of recipients (65%) receive tacrolimus, MMF and steroids as maintenance immunosuppression
- Only 6% of recipients were on cyclosporine-based immunosuppression, and 17% received the mTOR inhibitor Rapamycin
- The percentage of patients on steroid-free maintenance immunosuppression has increased from 4% in 2,000 to 24% in 2004, increase related to use of depleting induction agents (Thymoglobulin and Alemtuzumab).

BONE MARROW AND STEM CELL TRANSPLANTATION

BRETT GLOTZBECKER, MD • EDWIN PASCAL ALYEA, III, MD

Background

- Curative therapy for patients with inborn errors of metabolism, bone marrow failure syndromes, immune deficiencies, and hematologic malignancies
- Increasing use of bone marrow and stem cell transplantation
- As of 2009, estimated 35,000 autologous and 30,000 allogeneic stem cell transplants/year

Definitions

Autologous Stem Cell Transplant

• Use of an individual's own hematopoietic progenitor cells to reestablish hematopoiesis after exposure to high doses of chemotherapy or chemoradiotherapy

Allogeneic Stem Cell Transplant

- Use of an HLA matched donor's hematopoietic progenitor cells
- Efficacy derived from (1) infusion of tumor free graft and (2) graft versus disease effect mediated by donor lymphocytes

Compariso	on of Autologous to Allogenic	Bone Marrow Transplantation	
	Autologous	Allogeneic	
Advantages	No need for HLA match	Graft vs. tumor activity	
	No need for immune suppres- sive medications	Stem cells free of tumor and unharmed by chemotherapy	
	Lower risk of complications	Lower risk of relapse	
Disadvantages		Donor availability	
		Risk of graft vs. host disease (GVHD)	
	Higher risk of relapse	Higher risk of complications	

Other General Considerations Stem Cell Source

- Peripheral blood results in faster count recovery
- Bone marrow and cord blood stem cells are also used
 - Cord blood stem cells recover slowly. Patients tend to be at greatest risk of complications resulting from prolonged neutropenia and immature T cell phenotype.
- Neutrophil engraftment
 - Absolute neutrophil count (ANC) ≥500 cells/μl on 2 consecutive days or 1,000 cells/μl on 1 d
- Platelet engraftment
 - Unsupported platelet count >20,000 cells/μl

Comp	arison of 3 Potentia	al Stem Cell Sou	rces
Characteristic	BM (Bone Marrow)	PBSC (Peripheral Blood Stem Cells)	UCB (Umbilical Cord Blood)
HLA matching requirements	≥5/6 or 9/10	≥5/6 or 9/10	≥4/6
Time to neutrophil engraftment	22–24 d	10–14 d	1 Cord – 40 d 2 Cords – 12–24 d
Cell dose (TNC)	≥3 × 10 ⁶ cells/kg recipient	≥6 × 10 ⁶ cells/ kg recipient	1.5–2 × 10 ⁷ cells/kg recipient
Time to identify and collect cells	~2 mo	~2 mo	<1 mo
Risk of acute GVHD	Intermediate	Highest	Lowest
Risk of chronic GVHD	<pbsc< td=""><td>Highest</td><td><pbsc< td=""></pbsc<></td></pbsc<>	Highest	<pbsc< td=""></pbsc<>

Indications

Malignant

• Acute lymphoblastic leukemia (ALL), acute myelogenous leukemia (AML), myelodysplastic syndrome (MDS), non-Hodgkin's lymphoma, Hodgkin's lymphoma, chronic myelogenous leukemia (CML), chronic myelomonocytic leukemia (CMML), neuroblastoma

Nonmalignant

• Bone marrow failure syndromes, hemoglobinopathies, immunodeficiencies

Complications

Infusion Reactions associated with Stem Cell Infusion

Fevers

- May be due to contaminated product, cytokines released during processing, or co-incidental coinfection
- If fevers >100.5, send blood cultures + stem cell cultures and start broad-spectrum antibiotics until cultures are negative

Dimethyl Sulfoxide (DMSO) Toxicity

- Autologous stem cells are routinely cryopreserved with DMSO
- Symptoms nausea, vomiting, headaches, dizziness, itching, erythema
- Signs hypotension, arrhythmias, anaphylaxis
- Laboratory abnormalities mild intravascular hemolysis due to remaining RBCs in marrow, RBC in urine, elevated LDH
- Treatment saline for volume expansion then dopamine drip for continued hypotension, if symptoms persist remove DMSO from product

Special Circumstances

- Patent foramen ovale in patients with elevated right-sided pressures, there may be right to left shunting of blood flow
 - Clinical scenario infusion of stem cell products may result in a paradoxical cerebral emboli due to cellular aggregation
 - Prevention standard blood filter for all stem cell products

Posttransplantation

Engraftment Syndrome

- Definition
 - Inflammatory condition that usually occurs within the first 2 wks
- Etiology
 - Related to the release of cytokines from engrafting neutrophils
- Symptoms
 - Fevers, cough, shortness of breath, or hypoxia
- Examination
 - Erythematous rash and peripheral edema suggestive of third spacing
- Imaging
 - Chest X-ray: bilateral infiltrates are common
- Differential
 - Diagnosis of exclusion
 - Other etiologies infection and hyperacute GVHD
- Treatment
 - Methylprednisolone various doses used; typically start at 1 mg/kg/d and taper over 7–10 d

Acute GVHD

- General
 - Most common morbidity of allogeneic stem cell transplantation
- Incidence
 - Standard prophylaxis (calcineurin inhibitor [CI] and methotrexate)
 - 10%–50% matched sibling; 50%–90% matched unrelated donors
- Onset
 - Within 100 d of transplantation
- Risk factors
 - Increasing HLA disparity, age of recipient and female donor
- Clinical
 - Principle target organs of acute GVHD are the skin, gut, and liver

Acute GVHD Scale Based on Signs/Symptoms by Organ System			
Organ	Stage	Description	
Skin	1	Maculopapular rash – <25% body surface	
	2	Maculopapular rash – 25%–50% body surface	
	3	Generalized erythroderma	
	4	Desquamation and bullae	
Gut 1 2 3 4	1	Diarrhea - >500 mg/d or >30 ml/kg	
	2	Diarrhea - >1,000 mg/d or >60 ml/kg	
	3	Diarrhea - >1,500 mg/d or >90 ml/kg	
	4	Diarrhea - >2,000 mg/d or >90 ml/kg or Severe abdominal pain with or without lleus	
Liver 1		Bilirubin 2.0-3.0 mg/dl; SGOT 150-750 IU	
		Bilirubin 3.1–6.0 mg/dl	
	3	Bilirubin 6.1–15.0 mg/dl	
	4	Bilirubin >15.0 mg/dl	

Acute GVHD Cumulative Grading Scale				
Overall Grade	1	II	III	IV
Skin	1–2	1–3	2-3	2-4
Gut	0	1	2-3	2-4
Liver	0	1	2-4	2-4
Karnofsky scale	90-100%	70-80%	5060%	30-40%

- Treatment
 - Corticosteroids most effective no standard dose
 - Grades II–IV GVHD Methylprednisolone 2 mg/kg/d
 - Some support 1 mg/kg/d in patients with less severe GVHD (Blood. 2009;113(13):2888)
 - Second agent if failure to respond to steroid therapy within 3–5 d
 - Phase 2 study suggested that complete remission (CR) rates and OS were highest and severe infection rates were lowest in the group who received mycophenolate mofetil when compared to etanercept, denileukin diffitox, or pentostatin (*Blood*. 2009;114(3):511)
- Prognosis
 - Grade I GVHD 75% long-term survival
 - Grade II GVHD 60%–70% long-term survival
 - Grade III GVHD 25% long-term survival
 - Grade IV GVHD 5% long-term survival

Infectious Complications Neutropenic Fever

- Definition
 - Single temperature of >38.3°C (101°F) OR
 - Sustained temperature >38°C (100.4°F) for more than 1 hr IN
 - Patient with an absolute neutrophil count (ANC) <500 cells/ μ l OR <1,000 cells/ μ l with an expected nadir of <500 cells/ml
- Treatment
 - Standard empiric therapy includes coverage for gram negative bacteria including Pseudomonas S 3rd generation cephalosporins or pcn and aminoglycoside
 - Patients who are colonized with *Staphylococcus aureus*, or significant skin breakdown S consider vancomycin
 - If febrile after 96 hrs on these agents, 1–3-beta-glucan and galactomannan (aspergillus) assay should be sent, and an antifungal agent should be started
 - Patients on piperacillin-tazobactam may have false positive galactomannan assays
 - Patients treated with IVIG or albumin may have false positive glucan tests
 - Granulocyte transfusions in granulocytopenic patients in whom gram-negative bacterial or fungal infections are not controlled by antimicrobials remain controversial and are not currently recommended

Infections

- Based on time posttransplant and if on medications to prevent or treat GVHD
 - Day 0–30
 - Infections related to conditioning therapies and neutropenia bacterial infections from the GI tract or catheter related, aspergillosis, candidemia

- Day 30–80
 - Opportunistic infections cytomegalovirus (CMV), PCP, toxoplasmosis, nocardia, aspergillosis
- Day 180+
 - Encapsulated organisms (streptococcus pneumoniae, haemophilus influenzae, klebsiella pneumoniae), varicella virus (VZV), pneumocystis jiroveci (PCP)
- Day 0-180+
 - Respiratory viruses parainfluenza, influenza, respiratory syncytial virus (RSV), adenovirus

Figure 1. Timeline for Typical Infections after Autologous Stem Cell Transplant

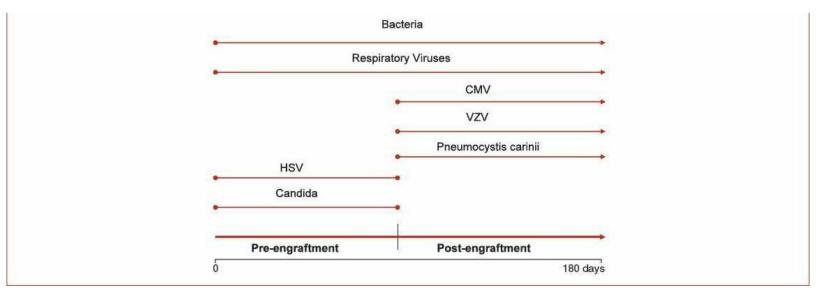
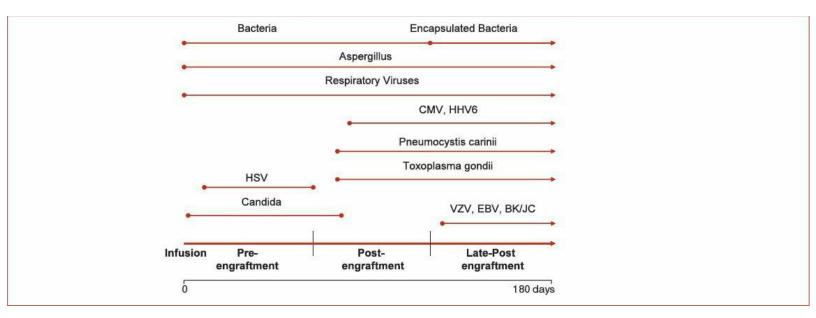


Figure 2. Timeline for Typical Infections after Allogeneic Stem Cell Transplant



- Risk factors
 - Neutropenia
 - Skin and mucosal lining breakdown and organ dysfunction
- Prevention
 - Broad-spectrum antimicrobial prophylaxis with at least a fluoroquinolone, acyclovir, and an antifungal

- Treatment
 - CMV disease (viremia + organ toxicity colitis/pneumonia)
 - Ganciclovir 5 mg/kg IV every 12 hrs until symptoms resolve and viral load negative × 2 S followed by suppressive dose valganciclovir 900 mg/d
 - IVIG 500 mg/kg 3 times/wk × 6 doses (may be useful in PNA)
 - *VZV*
 - Treat with acyclovir and VZIG or treatment doses of valacyclovir within 96 hrs of exposure
 - Limited involvement disease
 - Valacyclovir 1,000 mg TID or famciclovir 500 mg TID
 - Disseminated VZV (or pulmonary or liver involvement)
 - Acyclovir 10 mg/kg IV TID
 - *Adenovirus* pharyngitis, pneumonitis, enteritis, hepatitis, hemorrhagic cystitis, or disseminated disease
 - No effective proven prophylaxis or treatment
 - Cidofovir 5 mg/kg IV qwk × 2 wks; followed by 4 doses every other week (prehydrate and administer probenecid prior to each dose) anecdotal reports (*Biol Blood Marrow Transplant*. 2007;13(1):74)
 - RSV Pneumonia causes high morbidity/mortality posttransplant
 - Aerosolized ribavirin 6 g daily over 18 hrs no longer felt to be useful
 - Consider IVIG 500 mg/kg QOD for 5-7 d
 - Influenza
 - For influenza A or B oseltamivir 75 mg PO BID
 - For influenza A only amantadine 100 mg BID or rimantadine 100 mg PO BID
 - *PCP*
 - High dose bactrim 15–20 mg/kg/d divided every 6–8 hrs + Prednisone 40 mg PO BID d 1–5, 40 mg daily days 6–10, then 20 mg daily days 11–21
 - Or Atovaquone 750 mg PO TID
 - Or Dapsone 100 mg daily + primaquine 15 mg daily
 - Candidemia
 - Echinocandins caspofungin 70 mg IV daily followed by 50 mg IV daily or micafungin 100 mg IV daily
 - Azoles fluconazole 800 mg load then 200–400 mg daily; voriconazole 6 mg/kg IV q12h for 2 doses then 3 mg/kg IV q12h
 - AmBisome 3–5 mg/kg/d IV over 120 min
 - Aspergillus
 - Azoles voriconazole (preferred) 6 mg/kg IV q12h for 2 doses then 3 mg/kg IV q12h
 - AmBisome 3–5 mg/kg/d IV over 120 min
 - Echinocandins should only be used in patients intolerant to voriconazole or AmBisome. No data for first-line use
 - Zygomycosis
 - AmBisome (preferred) 3–5 mg/kg/d IV over 120 min. Dose could be increased to 7.5–10 mg/kg
 - Azoles posaconazole 800 mg/d divided BID or QID only use as salvage or step down treatment

Hepatic Complications Hepatic Veno-occlusive Disease (VOD)

- Alternative name
 - Sinusoidal obstruction syndrome
- Incidence
 - 5%–60% of patients following stem cell transplantation
 - More common after allogeneic transplants
 - Usually occurs day 0-day 30, but may be as late as day 50
- Etiology
 - Initial: endothelial injury of the sinusoids of hepatocytes in zone 3
 - Cascade of events including thickening of the subintimal zone of the sublobular venules leading to hepatic congestion, hepatocyte necrosis and centrilobular sinusoidal fibrosis
- Risk factors
 - Pre-transplantation related factors:
 - Liver dysfunction, history of viral hepatitis, prior liver radiation, tumor in the liver, estrogen use, iron overload, recent gemtuzumab ozogamicin use, previous transplant
 - Transplantation related factors
 - High-dose conditioning regimens including TBI or busulfan (with cyclophosphamide), sirolimus use in combination with high-dose conditioning, allogeneic donor
- Clinical criteria for diagnosis of VOD
 - Seattle criteria
 - Presence before day 30 of 2
 - Hyperbilirubinemia (>2 mg/dl)
 - RUQ pain/hepatomegaly
 - Ascites \pm weight gain >2% baseline
 - Baltimore criteria
 - Bilirubin ≥ 2 mg/dl by day 21 + at least 2
 - Hepatomegaly
 - Ascites
 - Weight gain >5% baseline
- Imaging
 - US with Doppler to look for reversal of flow/ascites
- Diagnosis
 - Liver biopsy and wedged hepatic venous pressure gradient gold standard
 - Risk in the setting of the patient being coagulopathic
 - Biopsy by the transvenous route
- Prevention
 - Use of ursodeoxycholic acid for prevention has been associated with a decreased incidence of VOD [6,7]. It is most effective if started 2 wks prior to conditioning therapy in patients at high risk of developing VOD.
- Treatment
 - Supportive diuresis, transfusion, CVVH, pain control
 - Investigational agent defibrotide treatment has been associated with day +100 posttransplant survival rates of 32–79% (*Biol Blood Marrow Transplant*. 2010;16(7):1005; *Oligonucleotides*. 2006;16(1):105; *Blood*. 2002;100(13):4337; *Blood*. 1998;92(3):737)

- Prognosis
 - 50–80% of patients symptoms resolve over 2–3 wks
 - Overall mortality is 20–50%

Pulmonary Complications

Idiopathic Pneumonia Syndrome (IPS)

- Definition
 - Widespread alveolar injury following SCT in the absence of lower respiratory tract infection and cardiac causes
- Incidence
 - Incidence is 3–15% with median time of onset at 6–7 wks
- Etiologies
 - Direct toxic effect of the conditioning regimens
 - Undiagnosed pulmonary infections
 - Release of inflammatory cytokines
 - Association between IPS and severe GVHD in several studies
 - IPS is less common after autologous HSCT
- Diagnostic criteria
 - Widespread alveolar injury (must meet all):
 - Multilobar infiltrates on chest radiograph or CT scan
 - Signs and symptoms of pneumonia
 - Evidence of abnormal pulmonary physiology (increased alveolar—arterial oxygen gradient OR the need for supplemental oxygen)
 - Absence of lower respiratory tract infection
 - Negative bronchoalveolar lavage or lung biopsy
 - Ideally negative test 2–14 d later
- Treatment
 - Optimal therapy unknown
 - Supportive therapy
 - Supplemental oxygen, mechanical ventilation
 - Empiric antibiotic coverage while awaiting culture data
 - Immunosuppressive Therapy
 - Corticosteroids (1–2 mg/kg/d for 3 d and taper by 50% every 3 d)
 - TNF-a inhibitor etanercept
- Prognosis
 - Mortality is 50%–85% in patients not requiring ventilation and ~95% in patients requiring ventilation

Diffuse Alveolar Hemorrhage (DAH)

- Definition
 - Acute form of noninfectious respiratory failure
 - Usually occurs within the first month of stem cell transplantation.
 - Incidence ranges from 1%–21% in autologous stem cell transplant
 - 2%–17% in allogeneic stem cell transplant recipients
- Etiology
 - Not well established

- Possible cytokine release by engrafting cells
- Diagnostic criteria
 - Multilobar pulmonary infiltrate
 - Symptoms and signs of pneumonia, and
 - Abnormal pulmonary physiology with increased alveolar to arterial oxygen gradient and restrictive ventilatory defect
 - Absence of infection compatible with the diagnosis
- Diagnosis
 - BAL with bloodier return from 3 subsegmental bronchi or
 - 20% or more hemosiderin-laden macrophages or
 - Blood in ≥30% of the alveolar surfaces of lung tissue
- Risk factors
 - Toxic effects of the conditioning regimens, older age, history of thoracic irradiation, and renal insufficiency
- Treatment
 - No prospective, randomized trials
 - Steroids 1,000 mg/d \times 3 d; taper by 50% every 3 d
 - Small studies of up to 2,000 mg steroids/day show no survival benefit (*Am J Respir Crit Care Med.* 2002;166(5):641)
- Prognosis
 - Majority require mechanical ventilator support
 - Reported mortality rate is between 64%–100%
 - Survivors do not suffer permanent respiratory compromise

Pulmonary Veno-occlusive Disease (VOD)

- Definition
 - Intimal proliferation of fibrous tissue in the pulmonary venules
 - Usually occurs 6–8 wks after stem cell transplantation
- Incidence
 - Very rare, incidence unknown as overlap exists with pulmonary HTN
- Etiology
 - Endothelial injury from infections, BCNU, and bleomycin
- Clinical features
 - Nonspecific dyspnea on exertion, lethargy, cough, chest pain, cyanosis, orthopnea, hemoptysis, DAH
- Diagnosis
 - Studies X-rays pleural effusions, Kerley B lines
 - Right heart catheterization difficulty obtaining pulmonary artery wedge pressure (if obtained normal or low)
 - Lung biopsy shows intimal proliferation
 - Presence of 20% or more hemosiderin-laden macrophages
- Risk factors
 - Exposure to BCNU, bleomycin
 - May be associated with hepatic VOD
- Treatment
 - Steroids 1–2 mg/kg/d anecdotal reports

- Prognosis grim
 - 2003 case report 40 patients 4 survivors (J Pediatr Hematol Oncol. 2003;25(5):405)

Neurologic Complications

Posterior Reversible Encephalopathy Syndrome (PRES)

- Etiology
 - Unique complication of calcineurin inhibitors
 - Often occurs in association with new onset hypertension
 - Development is not directly correlated with drug level
 - Cessation of the drug does not always lead to resolution
- Symptoms
 - Insidious onset of headache, confusion or decreased consciousness, visual changes, cortical blindness, or seizures
- Radiographic evaluation
 - MRI white matter edema in the posterior circulation
- Treatment
 - Changing to another agent such as mycophenolate mofetil
 - Blood pressure control is crucial
- Prognosis
 - The majority of cases are reversible within days to weeks with withdrawal of the inciting agent and blood pressure control
 - MRI findings of hyperintense signals on DWI or more extensive brainstem involvement predicts worse or irreversible outcomes

CNS Infections

- Toxoplasma gondii
 - Incidence
 - Up to 1.4% in centers with high seroprevalence
 - Occurs within the first month of transplantation
 - Clinical
 - Focal neurologic symptoms and encephalopathy
 - Radiology
 - MRI multiple mass lesions in the basal ganglia that are typically enhancing but in this population may be non-enhancing or hemorrhagic
 - Diagnosis
 - PCR on the CSF for *T. gondii* may also be positive
 - Treatment
 - Combination pyrimethamine, sulfadiazine, and folinic acid
 - Prognosis
 - Poor 1997 review of 55 cases, all but 1 fatal (Bone Marrow Transplant. 1997;19(7):685)
 - 2003 review of European Group for Blood and Marrow Transplantation data suggests with appropriate therapy up to 40% clinical or radiographic response
- CNS aspergillosis
 - Clinical
 - Angioinvasive fungal disease
 - New stroke-like symptoms or meningeal symptoms in addition to headaches, focal neurologic

signs or seizures

- Radiology
 - MRI lesions are often associated with edema, hemorrhage, infarction, and ring enhancement
- Diagnosis
 - Evaluation of spinal fluid is usually not helpful
- Risk factors
 - Early posttransplant (<40 d) age, HLA mismatch
 - Late posttransplant (>40 d) GVHD, CMV infection
 - Any time point neutropenia, lymphopenia, iron overload
- Treatment
 - Antifungal +/- neurosurgical procedure
 - Voriconazole achieves CSF levels S trough plasma levels
 - Retrospective study suggested lack of clinical efficacy for CNS aspergillosis with amphotericin B
- Prognosis
 - With use of voriconazole +/- neurosurgical procedure, reports of survival rates of $\sim 20\%$ (Blood. 2005;106(8):2641)
- Viral Encephalitis
 - Etiology
 - Human herpesvirus-6 (HHV-6)
 - Clinical
 - Limbic encephalitis
 - Short-term memory loss, seizures, confusion, and behavioral changes
 - Radiology
 - MRI hyperintense T2 lesions in the medial temporal lobes primarily in the hippocampus and amygdala
 - Diagnosis
 - PCR of the CSF for HHV-6 variant B
 - Treatment
 - Foscarnet
 - Other considerations
 - Consider PCR on the CSF HSV and VZV (reactivation less common in the era of acyclovir prophylaxis)
- Progressive Multifocal Leukoencephalopathy
 - Etiology
 - JC virus
 - Clinical
 - Motor deficits, limb or gait ataxia, and visual symptoms
 - Radiology
 - MRI increased signal on T2-images bilaterally in the periventricular regions and subcortical white matter
 - Diagnosis
 - Gold standard for diagnosis is brain biopsy
 - PCR can be sent on CSF for JC virus
 - Treatment

- Steroids or calcineurin inhibitors should be stopped
- No other proven efficacious treatment
- Prognosis
 - Usually progressive and often fatal

Renal Complications

Posttransplant Thrombotic Microangiopathy (TMA)

- Incidence
 - 0.5%–76% in different series (no uniform definition)
- Etiology
 - Multifactorial factors that damage endothelium, calcineurin inhibitors, sirolimus, chemotherapy and/or total body irradiation, stages III/IV GVHD, hepatic VOD, and fungal/bacterial infections
- Clinical
 - Clinical spectrum of TTP/HUS syndromes
 - One of the causes of acute and chronic kidney injury
- Diagnostic criteria
 - De novo prolonged or progressive thrombocytopenia, defined as a platelet count $<50,000/\mu l$ or $\ge 50\% \le$ previous values
 - RBC fragmentation ≥2 Schistocytes/high powered field
 - Decrease in hemoglobin or increase in transfusion requirement
 - Decreased haptoglobin
 - Persistently and unexplained elevation in LDH
- Treatment
 - Reduce or stop calcineurin inhibitors
 - Plasmapheresis for posttransplant TMA unlike in idiopathic TTP is controversial and has not proven to be effective (*Biol Blood Marrow Transplant*. 2005;11(8):571)
- Prognosis
 - With intervention, recovery of renal function in ~90%

Acute Renal Failure (ARF)

- Incidence
 - 42%–84% after myeloablative allogeneic stem cell transplant
 - Usually occurs within the first month following transplant
- Etiology
 - Infections CMV, BK
 - Post transplant complications GVHD, VOD, TTP
 - Medications calcineurin inhibitors, antibiotics/antifungals
 - ATN
- Diagnostic criteria
 - Rise in creatinine 2 × baseline/decrease in CrCL to 50% baseline
- Treatment
 - Depends on etiology stop possible causative agent; start fluids if secondary to volume depletion; treat possible infection
 - BK virus nephropathy unclear benefit of cidofovir, leflunomide, fluoroquinolone
 - Hemodialysis
- Prognosis

- Mortality is 2–3 times higher in patients with ARF
- If patients need dialysis, mortality rates may rise to >80%

Cardiac Complications

Arrhythmias

- Incidence
 - Relatively uncommon 2%–10%
 - Usually occurs during conditioning, DMSO infusion or first 1–2 wks after transplant
- Etiology
 - Conditioning cyclophosphamide, infection, volume overload, electrolyte abnormalities, DMSO, thyroid disease
- Diagnoses
 - ECG, electrolyte panel, TSH, +/- echocardiogram
- Treatment
 - If due to DMSO, slow the rate of infusion, hydrate and observe. If severe, give diphenhydramine and hydrocortisone
 - If atrial fibrillation with rapid ventricular response and uncontrolled by treating infection, repleting lytes, fluids; consider IV lopressor first (amiodarone/diltiazem are metabolized by the CYP450 and interact with many agents used in transplant)
- Prognosis
 - Permanent antiarrhythmic is usually not needed (*Bone Marrow Transplant*. 2004;34(7):615)

Myopericarditis

- Incidence
 - Cyclophosphamide toxicity is idiosyncratic
 - Occurs within 1–10 d of cyclophosphamide or infection
- Etiology
 - Cyclophosphamide, infection
- Syndromes
 - Severe associated with high doses tamponade and PEA arrest
 - Moderate congestive heart failure symptoms
 - Mild myocardial edema reduction in ECG voltage
- Clinical manifestations
 - Shortness of breath, pleuritis, cough, fevers, tachycardia
- Diagnoses
 - Physical exam pericardial rub
 - ECG diffuse ST segment elevation, PR depression, decreased voltages in the precordium
 - Echocardiogram effusion, tamponade, diastolic indentation or collapse of the right ventricle
 - Pericardial biopsy or aspiration of fluid
- Treatment
 - Stop possible causative agent; treat infection
 - If due to cyclophosphamide, no specific intervention
 - No NSAIDs if thrombocytopenic
 - Pericardiocentesis or pericardial window for tamponade
- Prognosis
 - Cyclophosphamide-induced myopericarditis commonly leads to asymptomatic effusion/ECG

voltage reduction
• Rarely toxic metabolites extravasate S myocyte necrosis/death

Transplant Related Complications

Summary of Transplant-Related Complications			
Organ System	Complication		
Immune	GVHD Engraftment syndrome		
Gastrointestinal	Hepatic veno-occlusive disease (VOD)		
Pulmonary	Idiopathic pneumonia syndrome (IPS) Diffuse alveolar hemorrhage (DAH) Pulmonary veno-occlusive disease (VOD)		
Renal	Thrombotic microangiopathy Acute renal failure		
Cardiac	Arrhythmia Myopericarditis		
Neurologic	Posterior reversible leukoencephalopathy		
	CNS infection (toxoplasma/aspergillosis/progressive multifocal leukoencephalopathy)		

PLASTIC SURGICAL CRITICAL CARE

J. RODRIGO DIAZ-SISO, MD • BOHDAN POMAHAC, MD

Skin Grafts, Pedicle Flaps Frequent Indications

- Breast
 - Mastectomy reconstruction (pedicle transverse rectus abdominis musculocutaneous flap)
- Head and Neck
 - Cancer reconstruction (pectoralis musculocutaneous flap)
- Trauma
 - Lower extremity trauma (gastrocnemius flap)

Monitoring

Clinical Assessment

	Healthy Flap	Compromised Arterial Flow	Venous Congestion
Skin color	Pink	Pale, mottled, bluish	Cyanotic, bluish
Temperature	Warm	Cool	Cool
Capillary refill	Normal (1–3 sec)	Sluggish	Brisk
Tissue turgor	Normal	Decreased turgor, flat appearance	Increased turgor, tense appearance
Pinprick test	Normal	Scant amount of dark blood	Rapid bleeding, dark blood

• Doppler Ultrasound

- Evaluates blood flow in major artery or vein of the pedicle
- Inexpensive, and easy to use
- False positive signals from arteries in the recipient bed or following venous obstruction

Free Tissue Transfer

- Transfer of distant tissues with their original blood supply
- Flap vessels connected to recipient site artery and vein(s) using microsurgical techniques

Frequent Indications

- Defects where local options are not available or remote donor site is preferable
 - Breast
 - Mastectomy reconstruction (DIEP flap)
 - Head and Neck
 - Cancer reconstruction (radial forearm fasciocutaneous flap)
 - Trauma
 - Lower extremity trauma (rectus or latissimus muscle flaps)
 - Donor Site Care and Morbidity

- Skin graft
 - Moist dressings facilitate healing and control pain
- Complications rare but possible
 - Infection
 - Delayed healing

POSTOPERATIVE MONITORING OF FREE FLAPS

Clinical Assessment – Same as Pedicled Flaps (see Table above)

- Gold standard
- Examination every hour post-op day 1
- Every 2 hrs post-op day 2–3; every 4–8 hrs thereafter

Handheld Doppler Ultrasound

- Most common device in use
 - Advantages
 - Can monitor both pulsatile-arterial and continuous-venous signals
 - Inexpensive, easy to use
 - Disadvantages
 - Unable to differentiate between recipient vessels and flap's vascular pedicle
 - Difficult to monitor buried flaps

Implantable Doppler

- Ultrasonic probe mounted on a silicone cuff; wrapped around venous pedicle and connected to a portable monitor
 - Advantages
 - Effective monitor of flap perfusion, especially in buried flaps
 - Easy to use by inexperienced clinical staff
 - Disadvantages
 - Costly
 - Probe may malfunction, or may be displaced during early post-op

Surface Temperature

- Monitored using probes, thermo-sensitive tape, non-contact thermometer, touch
 - Advantages
 - Surface temperature is easily taken
 - Required equipment is inexpensive
 - Of value when monitoring replanting digits
 - Disadvantages
 - Skin temperature reacts slowly to vascular occlusion
 - Inadequate indicator of intrinsic flap failure

Color Duplex Ultrasound

- Records blood flow velocity and blood flow direction
 - Advantages
 - Noninvasive, safe and quick, highly accurate
 - Works well in buried flaps, head and neck reconstructions
 - Disadvantages

- High cost of equipment, monitoring is not continuous
- Requires experience with device/licensed technician

Near-infrared Spectroscopy

- Uses principles of optical spectrometry
- Measures oxygenation, hemoglobin content in local tissues

Advantages

- Noninvasive, safe and quick
- Identifies early thrombosis before onset of clinical signs of flap failure
- Can distinguish between arterial, venous, and total vascular occlusion

Disadvantages

• High cost of equipment

Licox Tissue Oxygenation

• A microprobe measures pO_2 in the flap $(p_{ti}O_2)$

Advantages

- Provides continuous monitoring
- Can differentiate between arterial pedicle failure (rapid $P_{ti}O_2$ drop) and venous thrombosis (gradual $P_{ti}O_2$ drop)

Disadvantages

- Invasive, costly equipment
- Only monitors tissue near probe, may not detect ischemia in other areas

Key Concepts when Monitoring Flaps

High Degree of Clinical Suspicion

- Low threshold for detection of flap failure and take back to the OR
- Local infections may cause late thrombosis

Consider Local Factors

Positioning

Avoid pressure to flap and pedicle

Dressings

- Mechanical compression of vascular pedicle may cause thrombosis
- Take down dressing at bedside

• Incision Release

- Prior to OR transfer
- May relieve compression from edema and/or hematoma

Immediate Transfer to Operating Room if Flap Failure is Suspected

- Venous occlusion slow onset; arterial occlusion rapid event
- Flap survival is higher in venous occlusion vs. arterial thrombosis
- If vascular compromise suspected, transfer to OR immediately for surgical re-exploration

Antithrombotic Therapy

• No ideal regimen, some agents effectively prevent thrombus formation

Heparin

- Use for primary thrombosis prophylaxis is rare (risk of hematoma formation)
- Used after re-exploration and thrombectomy

Dextran

• Short term increase in patency of microcirculation

• Increased risk of hemorrhage, anaphylaxis, cardiac overload, renal damage

• Aspirin

- Prevents venous thrombosis
- Improves microcirculatory perfusion

Vascularized Composite Allotransplantation (VCA)

- Tissues of multiple histologic origins are transplanted from one donor to recipient
- Restores form and function of severe disfigurement that cannot be reconstructed with conventional reconstructive techniques

Indications

- Face Transplantation
 - Severe facial defect with loss 25% of facial surface, or one or more facial unit

• Upper Extremity Transplantation

• Bilateral or dominant upper extremity amputation

Other VCA Applications

- Abdominal wall transplantation
- Larynx/trachea transplantation

• Rationale

• Conventional reconstructive techniques are unable to fully restore the unique function and appearance of the face and upper extremity

• Unique VCA Considerations

- CTA combines techniques of reconstructive microsurgery and transplant surgery
- CTA patients are free flap and transplant patients

• Immunosuppressive Therapy

- Goal: optimize dose that will effectively avoid immune rejection (underimmunosuppression) and infections (overimmunosuppression)
- Regimens for VCA are in experimental phases

Common Side effects

• Nephrotoxicity (calcineurin inhibitors), hyperglycemia (steroids), bone marrow suppression

• Immune Rejection

• While adjusting immune suppression regimen, may get acute rejection

Clinical Assessment

• Allograft

• Erythema, edema

• Sentinel Flap

- VCA patients may have sentinel allograft flaps to aid monitoring and confirm onset of acute rejection
- Biopsies can be performed on sentinel flap to avoid scarring on facial allograft, but results may not correlate with facial skin/mucosa
- True value of sentinel flaps is unclear

Pathology

- Banff classification grades I–IV
- Topical treatment for grade I, systemic treatment for grades II–IV

• Treatment

- Topicals: steroid or tacrolimus creams in alternating sequenceSystemic: pulse of steroids

THORACIC SURGICAL CRITICAL CARE

SHANNON S. MCKENNA, MD

Postoperative thoracic surgery patients may require ICU admission based on either the type of surgery or underlying medical disease.

- Surgery: esophagectomy, pneumonectomy, extra-pleural pneumonectomy, radical pleurectomy, decortication, sleeve lobectomy, lung transplantation
- Co-morbidity: severe COPD, pulmonary HTN, significant CAD, aortic stenosis, empyema, severe restrictive lung disease
- Certain problems are commonly seen in the Thoracic ICU. Atelectasis, pneumonia, and respiratory failure are the most common complications after thoracic surgery.

PREVENTION/TREATMENT OF ATELECTASIS AND SECRETION RETENTION

- Contributing factors: splinting from pain, chest wall instability, diaphragmatic dysfunction, airway anastomoses, respiratory depression from opiates, COPD, pneumonia
- Consequences: hypoxia, hypercarbia, limited exercise tolerance, pneumonia, mediastinal shift
- Treatment:
 - Recruitment of lung volume: cough and deep breathing, ambulation, chest physiotherapy, incentive spirometry, effective pain control, IPPV
 - Cough assistance: chest physiotherapy, in-exsufflator, vibratory vest, acapella device
 - Secretion management: humidified oxygen, nebulized saline, inhaled N-acetylcysteine, inhaled dornase, antibiotics for pneumonia or bronchitis, fiberoptic bronchoscopy

POSTOPERATIVE HYPOTENSION

• Etiology can be broken down into: pump dysfunction vs. inadequate venous return; universal vs. patient population-specific causes

Causes of Hypotension in Thoracic Surgical Patients			
Non-Specific Causes	Medical Causes Associated with Thoracic Surgery	Mechanical Causes Associated with Thoracic Surgery	
Dehydration	Pulmonary HTN with right heart failure	Dynamic hyperinflation	
Hemorrhage	Sympathectomy (epidural induced or mechanical)	Tension hemothorax or hydrothorax (chyle leak; infection)	
Myocardial ischemia/ dysfunction	Atrial fibrillation	Mediastinal shift	
Sepsis		Cardiac herniation	
Pulmonary embolism			
Tension pneumothorax			
Cardiac tamponade			

• Management: find the specific etiology! EKG, CXR and ECHO can be very helpful

POSTOPERATIVE ACUTE RESPIRATORY DISTRESS SYNDROME

Epidemiology

- Incidence 4%–5% for pneumonectomy (right > left); 2% for lobectomy
- Mortality >50%

Pathophysiology

• Diffuse inflammatory process involving neutrophils, macrophages, endothelial injury, and platelet aggregation

Proposed Triggers for Lung Injury	
Ventilator-associated lung injury	
Oxygen toxicity	
Tissue injury with cytokine release	
Loss of lymphatic drainage	
Pulmonary hypertension	
Endothelial damage from increased blood flow	

Management

- Mirrors standard ARDS management (see Chapter 5)
- May be complicated by chronic air leaks or bronchial suture lines that limit achievable/desirable airway pressures; bronchial stump may break down in the setting of critical illness leading to proximal bronchopleural fistula (BPF) (see below)

MASSIVE HEMOPTYSIS

- Defined as >600 ml of blood in 24 hrs
- Death is by asphyxia not exsanguination

Causes of Massive Hemoptysis	
Pulmonary infection	
Bronchiectasis	
Tumor eroding into a bronchial or pulmonary artery	
PA rupture from Swan-Ganz catheter	
Trauma to chest	
Pulmonary hypertension	
Primary vascular abnormality (AVM, aneurysm, vasculitis)	

Management: Protect the Good Lung and Stop the Bleeding

- Turn bleeding side down
- Isolate non-bleeding lung: mainstem intubation of good lung, bronchial blocker placed in bleeding lung, double lumen endotracheal tube placement
- Bronchoscopy, CT, or angiography to determine site of bleeding
- Treatment: bronchoscopy base therapies, embolization, radiation, surgical resection

BRONCHOPLEURAL FISTULA

• Proximal (large airway open) or distal (lung surface injury)

Causes of BPF			
Proximal Distal			
Breakdown of bronchial stump	Alveolar rupture		
Breakdown of airway anastomosis	Persistent air leak after resection		
Traumatic injury to conducting airway	Traumatic injury of lung parenchyma		

- Risk factors for stump breakdown: technical error, empyema or pneumonia, irradiation, recurrent tumor, malnutrition, poor wound healing
- Consequences of proximal BPF: soilage of good lung, airflow preferentially via BPF, development of empyema
- Mechanical ventilation with proximal BPF: may need to exclude the BPF (endobronchial intubation); if not excluded pressure modes of ventilation may work better
- Mechanical ventilation with distal BPF: gas lost through chest tube participates in gas exchange; reported (expiratory) tidal volumes and minute ventilation underestimate alveolar ventilation; target inspiratory volumes instead

Pulmonary Hypertension Leading to Right Heart Failure (*ccm.* 2007;35:2037)

- Risk factors: COPD, interstitial lung disease, s/p pneumonectomy, ALI with severe hypoxemia, PE
- Signs/symptoms: hypotension, oliguria, acidosis, increased CVP, peripheral edema, hepatic engorgement/dysfunction
- Assessment: EKG for ischemia, ECHO, CXR, right heart catheterization
- Treatment: initially aimed at minimizing PVR and supporting right ventricle

- Treat reversible causes of increased PA pressures: hypoxia, hypercarbia, acidosis, fever, pain, hypervolemia, pulmonary hyperinflation
- Pharmacologic support of RV: inodilators (dobutamine and milrinone) provide inotropic support while decreasing PVR; inotropes (epinephrine, dopamine, norepinephrine) provide inotropic support but may increase PVR
- Pharmacologic therapies to decrease PVR: systemic nitrates (cause hypotension), systemic prostacyclin (cause hypotension), inhaled prostacyclin, inhaled nitric oxide, sildenafil

ATRIAL FIBRILLATION

- Incidence: 13%–44%; highest for pneumonectomy
- Purposed etiologies: atrial stretch, myocardial ischemia, pulmonary hypertension, electrolyte imbalance, vagus nerve irritation, high catecholamine levels
- Prophylaxis: beta blockers and calcium channel blockers reduce incidence
- Treatment:
 - Rate control
 - Rhythm control typically not successful acutely
 - By 6 wks most patients back in sinus rhythm
 - Atrial fibrillation induced hypotension usually improves when rate slowed
 - Beta blockers and calcium channel blockers mainstays; amiodarone, digoxin and sotalol have a role in some patients
 - Control of precipitating factors: pain, agitation, hypervolemia, hypokalemia, hypomagnesemia, hypoxia and hypercarbia leading to pulmonary hypertension or myocardial ischemia, respiratory distress
 - Anticoagulation: if in atrial fibrillation for more than 48 hrs and not contraindicated

PAIN MANAGEMENT

- Critical to prevent atelectasis, pneumonia and alveolar hypoventilation
- Pain sources: skin/soft tissue, ribs, intercostal nerves, pleura, pulmonary parenchyma
- Afferent pathways: intercostal nerves, phrenic, and vagus
- Treatment modalities for thoracic surgical pain: thoracic epidural, intercostal nerve block, paravertebral block, incisional catheters, systemic opiates, NSAIDs, acetaminophen, lidocaine patches
- Thoracotomy pain typically requires multi-modality approach; care must be taken to evaluate potential side effects in each patient before prescribing any given treatment

VASCULAR SURGICAL CRITICAL CARE

SHERI BERG, MD • RAE ALLAIN, MD

PERIOPERATIVE RISK

- Open aortic procedures and peripheral vascular surgery are "high risk" (>5%) for nonfatal MI or cardiac death (*Circulation*. 2007;116:e418).
- Common comorbidities include: coronary artery disease, congestive heart failure, hypertension, COPD, diabetes

CAROTID ARTERY STENOSIS

- Risk for stroke
- If severe (>70%) or symptomatic, indication for carotid endarterectomy (CEA) or stenting **Complications of CEA** (*Br J Anaesth*. 2007;99(1):119; *J Cardiothoracic Vasc Anesth*. 2009;23(2):245)

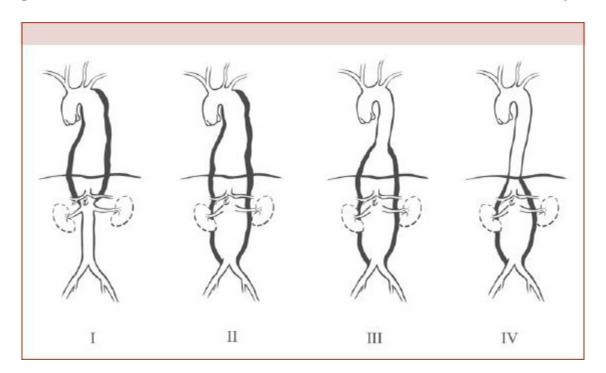
Neurologic	Cardiac	Airway/Pulmonary
Stroke: 3.4% (due to clamping, thromboembolic events or hemorrhage) Cerebral hyperperfusion syndrome: 0%–3% (increase in ipsilateral perfusion after flow through the carotid artery is reestablished – can lead to cerebral edema and death Cranial nerve injury (majority transient)	Myocardial infarction: 2.2% Bradydysrhythmias and hypotension (from manipulation of the carotid sinus) Hypertension	Obstruction/tracheal compression (results from an expanding neck hematoma and can be fatal if not immediately recognized) Hypoxia and hypercarbia (due to dysfunction of the carotid body chemoreceptors) Hoarse or weak voice (due to vagus nerve injury)

Carotid stenting is less invasive than CEA, possibly preferred for difficult anatomy (prior surgery/radiation) or multiple comorbidities, but higher risk for stroke (New England Journal of Medicine. 2010;363:11)

AORTIC ANEURYSMS (Circulation. 2005;111(6):816)

Types of Aortic Aneurysms				
	Ascending	Descending Thoracic/ Thoracoabdominal	Abdominal	
Etiology	Cystic medial degeneration	Atherosclerotic deposits	Atherosclerotic deposits	
Risks	Hypertension and Marfan's syndrome, syphilis	Smoking, hypertension, age, hyperlipidemia	Smoking, hypertension, age, hyperlipidemia	

Figure 1. Crawford Classification of Thoracoabdominal Aortic Aneurysms



Surgical Approach to Aortic Aneurysm Repair

- Endovascular approach most common for infrarenal AAA
 - Mortality < 2%
 - Fewer complications
 - Usually no need for ICU, except in case of thoracic endovascular stent placement, where risk of spinal cord ischemia may merit close neurologic monitoring +/- lumbar spinal catheter for CSF drainage (*Br J Radiol.* 2002;75:700; *J Vasc Surg.* 2011;53(1):187; *JAMA.* 2009;302(14):1535)
- Open approach indicates more complex anatomy
 - Mortality >4.5%
 - May include visceral arterial reconstruction
 - Greater blood loss/fluid shifts (JAMA. 2009;302(14):1535; J Vasc Surg. 2004;39(3):497)

Complications (Ann Thorac Surg. 2007;83:s856; J Vasc Surg. 2004;40:36; Ann Thorac Surg. 2007;83:s877; Anesth Analg. 2010;111:46)

- Cardiovascular
 - MI
 - Dysrhythmias
 - CHF
- Pulmonary
 - Pneumonia
 - Paralyzed hemidiaphragm due to phrenic nerve injury, division of diaphragm
 - Prolonged respiratory failure
- Renal
 - Ischemic nephropathy
 - Contrast induced nephropathy
 - Cholesterol embolization injury
- Hematologic
 - Massive hemorrhage

- Coagulopathy
- DIC
- Neurologic
 - Delirium
 - Spinal cord ischemia (anterior spinal artery syndrome) due to interruption of critical vessels supplying the spinal cord; most commonly arising from T7-L1

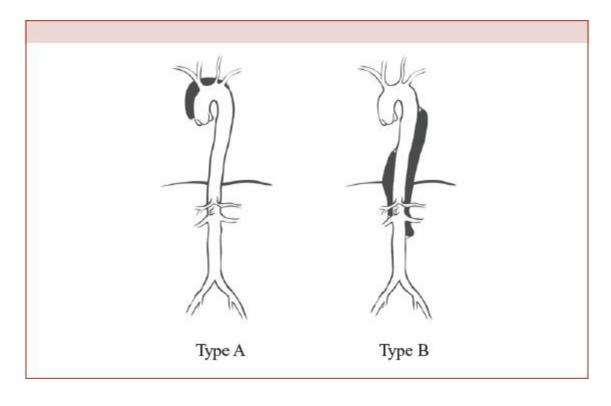
Intra- and Post-operative Management

- Invasive hemodynamic monitoring
- Appropriate fluid and blood product administration
- Beta blockers (when euvolemic) beneficial due to prevalence of CAD
- Postoperative mechanical ventilation may be necessary
- Tracheostomy for prolonged respiratory failure
- Avoidance of secondary renal injury (hypovolemia, hypotension, nephrotoxic medications, iodinated contrast)
- Renal replacement therapy may be required
- Induced hypertension and CSF drainage via lumbar spinal drain indicated for anterior spinal artery syndrome

AORTIC DISSECTION

- Etiology is a tear in the intima of the vessel wall which allows blood to flow between the layers of the aorta, creating a "false" lumen (*Crit Care Clin*. 2007;23(4):779)
- Risks are hypertension, connective tissue disorder (Marfan's, Ehlers–Danlos), bicuspid aortic valve, massive blunt chest trauma

Figure 2. Stanford Classification of Aortic Dissection



Diagnosis

Diagno	ostic Modalities for Ruptured Aortic Aneurysms		
Chest X-ray Widened mediastinum; aortic "knob"			
+ (Contrast) CT scan	Contrast delineates 2 lumens, initiation point, and extent of dissection		
MRI	Gold standard; 3D reconstruction		
TEE	Real time viewing; color Doppler allows for visualization of flow and dynamic components of flow in true/false lumens		

Treatment (Crit Care Clin. 2007;23(4):779; J Thorac Cardiovasc Surg. 1965;49:130; J Cardiovasc Surg. 2010;51(5): 641; Nat Rev Cardiol. 2011;8(2):103)

Treatment Options for Dissected Aortic Aneurysms				
Medical	Surgical/Definitive			
Preferred for Stanford B Control blood pressure to minimize dissection propagation: β blockers, CCB, vasodilators	Preferred for Stanford A due to high mortality (30% at 48 hrs) May be required for Stanford B if evidence of malperfusion (gut, kidneys, limbs) or pending rupture Endovascular options increasingly considered			

PERIPHERAL VASCULAR DISEASE

- Etiology is atherosclerosis, similar to what occurs in the heart and in the aorta
- Claudication is usually the presenting symptom
- Treatments include angioplasty, stenting, or open surgery to improve or divert flow to affected areas
- ICU care generally reserved for open procedures (femoral—popliteal or femoral—tibial bypass graft) with need generally correlating to duration of surgery and underlying comorbidities

Complications: (Semin Cardiothorac Vasc Anesth. 2004;8:335)

Тур	oical Complications of Peripheral Vascular Disease
Sepsis	"Septic Limb" should be treated by emergent surgery for source control
Rhabdomyolysis	Compartment syndrome can develop if a graft is occluded or kinked, or if there is ongoing ischemia to the limb
Death Most commonly due to cardiovascular morbidity	

NEONATAL INTENSIVE CARE

STEVEN A. RINGER, MD, PhD

RESUSCITATION IN THE DELIVERY ROOM

Apnea is the Hallmark Sign of Neonatal Depression

Primary apnea: occurs shortly after a stress or insult to the baby, and is easily corrected with stimulation

- Primary apnea (untreated) will progress through period of gasping to Secondary apnea
- Secondary apnea requires vigorous resuscitation, including the provision of positive pressure breaths

Primary and Secondary Apnea May Initially Appear Similar

They cannot be distinguished by relation to delivery, as both may occur before, during, or after birth.

Therefore: always assume that apnea is secondary and be prepared to intervene

IF BABY IS APNEIC OR THE HR IS LOW, the priority is to establish the airway and breathing. Until this is done, chest compressions and medications are of little or no value!!

Situations where the likelihood of needing resuscitation is increased:

- Prematurity
- Evidence of non-reassuring fetal status
 - Category 3 (i.e., abnormal) tracing of fetal heart rate
 - Persistent bradycardia
- Known or suspected anomalies
- Meconium-stained amniotic fluid
- Maternal conditions with potential effect on transition from fetal to newborn life
- Factors associated with an increased risk of infection in the newborn
- Abnormal delivery shoulder dystocia, breech, or abnormal lie

Preparation

• Ensure that all resuscitation equipment is functional

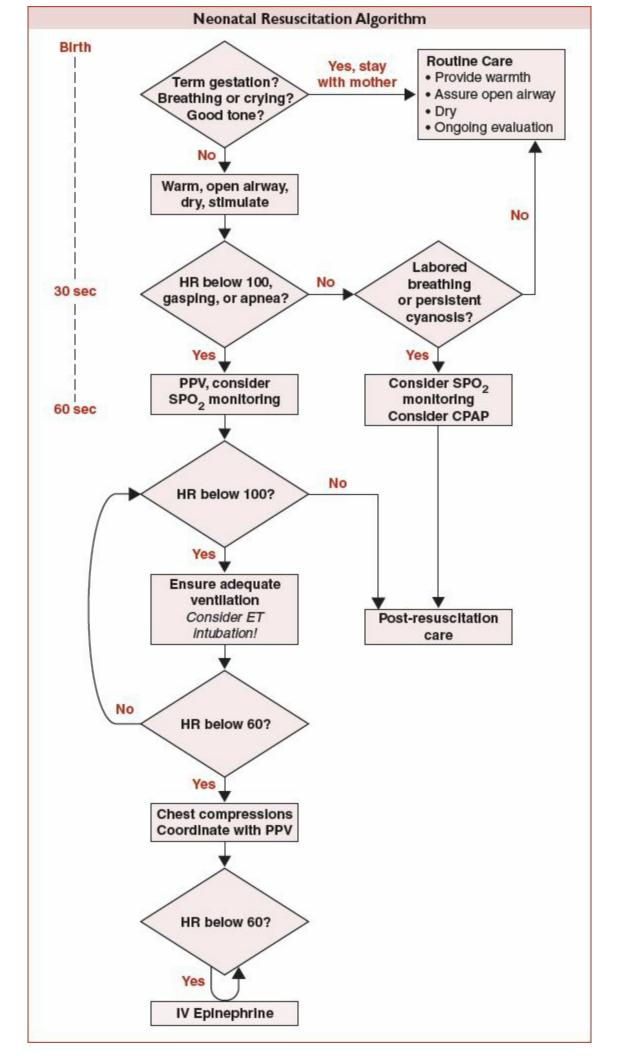
Upon receiving the infant

- Place him/her on radiant warmer, GENTLY DRY BABY
- Very low birth weight (VLBW) infants should be placed UNDRIED (head exposed) in plastic wrap/bag
- Discard wet towels
- Position head in slight extension, midline
- Suction mouth, and then the nose with bulb, **ONLY IF NEEDED**
- If there is meconium-stained fluid, evaluate:
 - Intubate and suction the trachea if the infant is not vigorous

- If the infant is vigorous, give routine care
- VIGOR = Good HR, good respirations, good tone
- Give tactile stimulation if apneic, repeat once (total of twice) if needed
 - Acceptable methods: rub back, flick soles of feet
- Apgar scores (see Table): Assign them at 1 and 5 min of life. Repeat every 5 min until ≥7

Apgar Scores						
Criterion	0	1	2			
Heart rate	0	<100	>100			
Respiration	None	Slow, irregular	Good cry			
Muscle tone	Limp	Some flexion	Active movement			
Reflex irritability	None	Grimace	Cough/sneeze			
Color	Blue, pale	Pink body	Pink			

• Repeatedly evaluate breathing, heart rate, color (in that order), and base decisions for intervention on this evaluation as follows:



Assess: Is the Baby Breathing?

- If the baby appears to be breathing, move to step 2
 - If infant remains apneic, give breaths by bag/mask until respirations are spontaneous
- For term babies start resuscitation with room air
- For premature infants <32 wks, start with blended oxygen 40%–60%
- For all babies, monitor oxygen saturation and adjust concentration to ensure target saturations. These are considered the same for babies of all gestational ages

Target Oxygen Saturation ("Pre-ductal" Measured on Right Upper Extremity)				
Time After Birth	Target Saturation (%)			
1 min	60–65			
2 min	65–70			
3 min	70–75			
4 min	75–80			
5 min	80–85			
10 min	85–95			

Positive pressure ventilation

- Indications:
 - Apnea
 - Heart rate <100 despite spontaneous respirations
 - Persistent poor color/low oxygen saturations
- Procedure
- Begin positive pressure ventilation (PPV) with bag and mask at 40–60 breaths/min. Use adequate pressure/volume so as to result in chest expansion
 - The first breath may require 30–40 cm H₂O
 - Subsequent breaths usually require 15–20 cm H₂O, but may require 20–40 cm H₂O in low compliance states (e.g., RDS)
 - Bag-mask ventilation is often as effective as intubation. If not, check:
 - Mask seal
 - Reposition head to ensure open airway
 - Suction the airway
 - Open the mouth slightly
 - Increase the pressure used
 - Consider an alternative airway
 - Intubation
 - Laryngeal mask airway (LMA) if baby is >1,500 g

Intubation

- Indications:
 - Known or suspected diaphragmatic hernia
 - To deliver meds (epinephrine) if vascular access has not been achieved
 - To give surfactant in infants <28 wks gestation
- Relative indications:
 - When PPV alone is not working

- Airway stability during resuscitation or transport
- Long-term ventilator support likely
- Need for PEEP
- Procedure see below
 - Limit duration of each intubation attempt to 20–30 sec
 - Check tube placement by auscultation over lungs and stomach, and presence of end-tidal CO₂

Assess: Once Ventilation is Assured (or Spontaneous) Check the Heart Rate

- Heart rate is an excellent indicator of the efficacy of resuscitative efforts
 - If HR > 100, monitor. If respiratory support has been needed, observe for spontaneous breaths
 - If HR < 100, or apneic, continue PPV as above, even if apparently breathing
 - If HR < 60 start chest compressions
 - Encircle chest with both hands, thumbs meet over lower sternum
 - Chest compressions are applied to the sternum below the nipple line at 90/min, depressing the sternum 1/2–3/4 in. Supplied breaths continue at 30/min during compressions
 - Total of 120 events/min
- Recheck HR every 45–60 sec to assess need for continuing compressions
- Give medications (below) if heart rate does not improve

Assess: Once Breathing and Heart Rate are Ensured, Assess Oxygen Level

- Clinical assessment of color is unreliable in the newly born infant
 - Pulse oximetry is more reliable, and can aid in heart rate monitoring
- Oxygen should be given in a concentration adequate to result in saturation within the target range for each minute after birth
- For infants >32 wks gestation, start in room air and titrate up as needed
- For preterm infants <32 wks gestation, use blended oxygen (40%–60%) and titrate up or down as needed

Medications

- If the heart rate remains <60 despite assisted ventilation, chest compressions and 100% oxygen, resuscitation medications are indicated
- Estimate patient weight at 1, 2, or 3 kg: 1 kg < 29 wks, 2 kg 29–33 wks, 3 kg 34 + wks
- Epinephrine: often give first dose by ETT (0.3–1.0 ml/kg) while awaiting, obtain vascular access. IV dose: 0.1–0.3 ml/kg. Always use 1:10,000 dilution
- Volume: 10 ml/kg of normal saline given IV. Can get emergency O negative blood if hemorrhage is known or suspected. Transfuse slowly

Resuscitation Medications in Delivery Room						
Med	Indication	Route	Dose	Comment		
Epinephrine	Low HR,	ET	0.3-1.0 ml/kg			
	Poor perfusion	IV	0.1-0.3 cc/kg q5min 1:10,000 dilution			
Volume	Volume loss, shock	IV	10 ml/kg	NS, blood Over 5 min		

• Drugs that are not used:

- Sodium bicarbonate is not efficacious and may be harmful
- Naloxone is not helpful. Apnea caused by maternal opioids should be treated with PPV

Stopping Resuscitative Efforts

- If, after 10 min of properly performed resuscitative efforts with good chest rise, the heart rate remains undetectable, it is reasonable to stop efforts
- In other clinical situations the benefits and risks of continuing resuscitation must be weighed when considering whether to continue efforts

Some Common Mistakes in Resuscitation Include

- Focusing on low heart rate rather than correcting apnea
- Failure to remove wet towels after drying the baby
- Failure to position the head in midline
- Flexion or hyperextension of the baby's neck during bag and mask ventilation
- Too small an initial breath, and too large subsequent breaths
- Tendency to bag-ventilate fast and shallow. AIM FOR RR of 40 (Count: Squeeze, two, three...)

The NICU: The Initial Workup

- Detailed maternal, obstetric, family history
- Physical examination:
 - Complete physical examination
 - Record the length, weight, and head circumference, and plot their percentiles
 - Dubowitz/Ballard examination to assess gestational age
 - Include retinal red reflex, hip examination for dislocation (even for prematures)
 - Number and type of umbilical vessels
 - Detailed neurobehavioral examination
- Laboratory data
 - Obtained as indicated by the clinical situation, none are routine
 - Common tests: include CBC w/diff, Ca, glucose, blood culture, type, and crossmatch
 - CSF studies: if indicated, it is optimal but not mandatory to obtain CSF before antibiotics have been administered
- Radiographs
 - If possible, have all central venous catheters and tubes in place before getting a radiograph to minimize radiation exposure
 - It is usually possible to accurately ascertain correct endotracheal tube (ETT) position by physical examination or CXR before surfactant therapy

Special Tests

- Newborn screen
 - Varies from state to state, but usually includes: phenylketonuria, maple syrup urine disease, homocystinuria, galactosemia, hypothyroidism, congenital adrenal hyperplasia, toxoplasmosis, hemoglobin electrophoresis, cystic fibrosis
 - Kleihauer–Betke test:
 - Detects fetal red cells in maternal blood (i.e., feto-maternal hemorrhage)
 - Maternal blood is fixed on a slide

- The adult hemoglobin is eluted with acid
- Fetal cells are visible after appropriate staining
- The size of the transfusion is estimated from the percent of fetal cells
- Apt test:
 - Determines whether gastrointestinal blood is fetal or maternal (swallowed during delivery or breast-feeding) blood
 - Will not work on stool

Common Procedures

- Thermal regulation: babies, especially prematures, will lose heat very rapidly while exposed for procedures. Heating lamps may be needed during initial evaluation; should be used unless the baby is big and the procedure very brief. Small babies should be admitted to humidified incubator ASAP
- Heelsticks: warm foot first, and avoid plantar aspect of foot. Electrolytes, Hct, BUN/Cr, capillary blood gases, some drug levels, bilirubin can be drawn this way. This method can give factitious results, especially if flow is poor. Hct may be 5%–15% higher than central venous Hct
- Venipuncture: usually a small rubber band will suffice as tourniquet. Blood obtained in this manner is good for most studies
- Scalp veins: avoid shaving the area if possible; combing is usually adequate. A rubber band placed around the head proximally is a helpful tourniquet
- Arterial puncture: useful for ABGs, or other tests if venipuncture is not possible and a moderate volume of blood is needed
 - Ensure collateral flow via ulnar artery before puncturing the radial artery. The newborn hand is usually ulnar predominant, thus damage to this vessel can have dire consequences
 - The angle of approach to the radial artery is very shallow, and is best accessed at the second subthenar crease
 - Transillumination of the wrist is often helpful
- Umbilical arterial catheter (UAC):
 - Great for monitoring ABGs and other labs, infusing parenteral nutrition, blood pressure monitoring
 - Use 2.5, 3.5 or 5F UAC catheter depending on baby size
 - Tip should be placed at T6–T10 ("high catheter") or L3-L5 ("low catheter")
 - The length of a high line is (approximately) umbilicus—shoulder distance + 2 cm
 - Sterile technique and X-ray to check line placement are mandatory
 - Do not administer vasopressors or platelets via UAC
 - Dwell time should be as short as possible, depending on clinical needs
 - Monitor legs, especially toes, for signs of vascular insufficiency or embolism (blue toes)
 - If present, warm other foot and consider pulling catheter. Monitor for hypertension or hematuria with a "high" UAC and remove the catheter
 - Feeding with UACs in place is a matter of controversy, although it is agreed that gut priming is not harmful
- Umbilical venous catheter (UVC):
 - Good for emergency access, exchange transfusions, monitoring of labs and CVP
 - Tip must be placed above liver (IVC-RA junction) if used for continuous infusions
 - This is roughly distance from umbilicus to lower sternum distance

- Dwell time should usually not exceed 10–14 d
- A "low" UVC can be emergently placed for emergency drug or fluid administration or for exchange transfusion
 - Insert catheter just to the point of blood return, usually 3–5 cm in term babies, 2–4 in preterm babies
 - Dwell time should be limited to the length of the emergent need
- Arterial catheters (line) (peripheral)
 - Not for infusion other than flushes, normal or half-normal saline or sodium acetate low-rate infusions
- Intubation:
 - Small straight laryngoscope blades (Miller 0 or 00 for prematures, Miller 1 for term) are used
 - Uncuffed ETT are almost always used, size
 - 2.5 for BW < 1,000–1,250 g
 - 3.0 for BW 1,250–2,000 g
 - 3.5 for 2,000+g
 - 4.0 for sometimes used in larger babies
 - Can be nasal assisted by Magill forceps or oral. Videolaryngoscopy is becoming available.
 - On radiograph, tip of ETT should be below clavicles (thoracic inlet) and above carina
 - Neonates are commonly intubated awake
 - In elective procedure, sedate with narcotic or benzodiazepine
 - The neonatal airway presents special difficulties:
 - Larynx is small, anteriorly and superiorly placed
 - Cricoid pressure is often useful in pushing the larynx into view
 - The tongue is relatively large and the epiglottis, which is omega shaped, may conceal the cords
 - Endotracheal tube position varies with head position: a flexed head results in a lower tube tip. "The hose goes with the nose!"
- Chest tubes: usual site of insertion is 4–5th intercostal space above rib, at anterior axillary line. Watch for and avoid nipples
- Bladder tap:
 - The suprapubic area is prepped in a sterile manner
 - A 22 or 23 gauge needle attached to a syringe is introduced at the midline above the pubic bone, and slid in up to 3 cm aiming at the coccyx. If no urine is obtained, the bladder is empty
 - Some advocate directing the needle straight downward
- Lumbar puncture:
 - The patient is placed in a lateral decubitus or sitting position, with the lower spine curved
 - The area is prepped and draped in a sterile manner
 - 22 gauge spinal needle with stylet is introduced between L3 and 14 or L4 and L5, above Touffier's line
 - The needle is advanced toward the umbilicus. A "pop" is felt as it enters the subarachnoid space
 - In premature infants this is only a few mm depth
 - CSF should be sent for culture and sensitivity, Gram stain, protein, glucose, cell count

COMMON NEONATAL PROBLEMS

Respiratory Disorders

Tachypnea: respiratory rate > 60/min

- Cold stress
- Sepsis/pneumonia
- Respiratory distress syndrome (RDS)
- TTN transient tachypnea of the newborn, due to retained fetal lung fluid
- Metabolic acidosis
- Polycythemia
- Anemia
- Hypoglycemia
- Congestive heart failure due to structural anomalies or patent ductus arteriosus

Respiratory failure:

- Diagnosed on clinical signs or defined as $pCO_2 > 55$, $pO_2 < 50$, pH < 7.25.
- Progression of treatment for hypoxemia
 - Give up to 60% oxygen by hood. If this is inadequate:
 - Begin CPAP (+ 4–6 cm water) Larger babies often tolerate this poorly
 - Skip trial of CPAP if there is decreased ventilation or respiratory distress
 - Intubation and mechanical ventilation. Also indicated for:
 - Severe apnea
 - Intractable seizures
 - Suspected persistent pulmonary hypertension (PPHN)
 - Surgical abdomen w/respiratory compromise
 - Conventional ventilation is usually tried first (synchronized intermittent mandatory ventilation SIMV). Often used in volume guaranteed mode.
 - High frequency ventilation (HFV) (high frequency oscillatory ventilation [HFOV] or high frequency jet ventilation [HFJV])
 - Failure of conventional ventilation modes:
 - HFOV useful for both hypoxemia and hypercarbia
 - HFJV often effective for hypercarbia, and air leak syndromes
 - Local practice may favor earlier use of HFV of one or both types
 - Inhaled nitric oxide used in conjunction with mechanical ventilation for PPHN
 - Extracorporeal membrane oxygenation (ECMO) may be effective in term and near-term infants for whom other modalities have failed
- Respiratory management of the newborn should be
 - Geared toward minimizing complications associated with hyperoxygenation and barotrauma or hyperventilation
 - Even short periods of low pCO₂ may be harmful
 - The neonate usually tolerates pH > 7.28, pCO₂ 45–55, pO₂ 45–65 very well and these can be used as weaning parameters
 - Typically weaning is done by
 - Decreasing FiO₂, then PIP
 - Specifics depend on the disease
 - For premature infants <32 wks who require supplemental oxygen, keep O2 saturation between 90–94%

• For more mature babies who require supplemental oxygen, keep oxygen saturations between 87%-97%

Respiratory distress syndrome

- Primarily a disorder of prematurity (also rarely in term babies)
- Underlying cause is deficiency (total or partial) of pulmonary surfactant, variable component of pulmonary hypertension
- Hypoxemia should be the major abnormality early on, if not, review diagnosis
- The pattern on CXR is usually a homogeneous "ground glass" opacification with air bronchograms
- Difficult to distinguish from Group B streptococcal (GBS) pneumonia
- In more mature babies, chest radiograph may be less homogenous, often patchy with air bronchograms
- Treatment:
 - Fluids are monitored closely, may need to slightly restrict until diuresis occurs
 - First line is oxygen supplementation for mild cases
 - Most babies require some end expiratory pressure CPAP is effective, especially when started as early as possible
 - Conventional ventilator management includes a high rate, lowest possible PIP, and low I-time
 - Typical initial settings: PIP 20–22 (use the lowest PIP that moves the chest well), PEEP 5–6, rate 30, FIO₂ to keep O₂ saturation as noted above
 - Exogenous surfactant is of benefit, and should be administered as soon as the diagnosis is made or highly suspected (soon after birth)
 - Babies of extremely low GA often receive surfactant immediately after birth if intubated
 - Repeated doses of surfactant, up to a total of four, are given if $FiO_2 > 0.3-0.35$, MAP > 8 at end of dosing interval. Need varies with product used
 - Additional doses often given to all extremely immature infants

Transient tachypnea of the newborn (TTN)

- Believed to be due to delayed resorption of fetal lung fluid
- Babies with TTN are usually mature, often born by cesarean section, especially those without labor. Please . . . NOTE that
- Tachypnea
- Mild cyanosis or low to moderate supplemental oxygen need
- Mild respiratory distress
- Typically improves in the first 4–6 hrs, and is usually resolved by 24 hrs after birth
- Chest radiograph
 - Prominent vascular markings
 - Fluid in fissures
- TTN is a diagnosis of exclusion; antibiotics should be considered in the absence of improvement or continued or increasing need for O_2 after first hours
- Rarely requires specific therapy

Persistent pulmonary hypertension of the newborn (PPHN)

- May develop after
 - Asphyxia, especially chronic
 - Aspiration, such as meconium-stained or clear amniotic fluid

- Pulmonary parenchymal or vascular disease or
- Pulmonary hypoplasia
- Congenital cardiac malformations
- Sepsis
- Persistent elevation in pulmonary vascular resistance results in:
 - Right to left shunting occurs at the level of the atria or ductus arteriosus
 - Cardiac dysfunction
 - Resultant hypoxemia
- Chest radiograph may be clear or show decreased pulmonary blood flow
- Oxygen saturations (and PaO₂) may show gradient between "pre-ductal" sites receiving arterial supply form vessels proximal to the ductus arteriosus (right upper extremity) and measurements made "post-ductal" (in left or lower extremities)
- Electrocardiogram may show RVH or strain, myocardial dysfunction, and a right to left shunt
- Structural heart disease should be ruled out
- Treatment:
 - The goal is to reduce pulmonary vascular resistance and decrease right to left shunting
 - May respond to administration of 100% oxygen
 - Systemic blood pressure should be supported with vasopressors as needed
 - Patient may be sedated or chemically paralyzed to prevent catecholamine release
 - Inhaled nitric oxide is mainstay of therapy, usually at 20 ppm to start
 - ECMO used in cases unresponsive to other therapies

Meconium aspiration syndrome (MAS)

- Chemical pneumonitis resulting from meconium aspiration before birth
- Results from hypoxemia-induced gasping
- Infection, PPHN often associated
- Often results in
 - Lower airway obstruction, air leak syndromes
 - Hypoxemia and decreased ventilation
- Radiograph
 - Heterogeneous, patchy, "snow storm" with areas of hyperinflation and atelectasis
- Treatment
 - Broad spectrum antibiotic coverage
 - Pulmonary toilet and close monitoring of respiratory status, blood pressure, calcium and glucose
 - Conventional ventilation may require high PIP, adequate PEEP, and longer expiratory time to avoid air trapping
 - High frequency ventilation for HFOV use lower Hz (6–12), higher amplitudes than used for pneumonia or RDS
 - ECMO for most severe cases
 - Concurrent treatment of PPHN as needed

Air leak

- Spontaneous (2%–3% incidence after normal births)
- Often due to excessive ventilation, progression of disease, and rarely due to trauma from procedure
- Prevention focuses on minimizing barotrauma by avoiding excessive PIP and PEEP
- Pneumothorax:

- Clinical signs
 - Decreased breath sounds
 - Sudden decompensation
 - Positive transillumination of chest
 - Asymmetry of chest
- Diagnosis confirmed by
 - Radiograph, or
 - Diagnostic needle aspiration
- Treatment
 - Not necessary in mild cases
 - Needle aspiration
 - Chest tube placement may be necessary if leak is recurrent or if lungs are abnormal/diseased
- Pulmonary interstitial emphysema
 - Air leak from alveoli into interstitium
 - Can cause cardiovascular and respiratory instability
 - Most severe form is air block, when interstitium is gas filled and alveoli are compressed
 - Clinical signs
- Worsening hypercapnia
- Decreased breath sounds
 - Radiograph confirms diagnosis
- Cystic bubbles radiating linearly from hilum
- Increased apparent lung size
 - Treatment is aimed at reducing mean airway pressure (MawP) and PEEP (often to very low levels temporarily)
 - HFJV
 - Rarely, extremely severe cases can be improved by placing affected lung in dependent position or selective intubation of unaffected side
- Pneumomediastinum
 - Diagnosis suggested by distant heart sounds, respiratory distress
 - Lateral chest X-ray is most helpful for diagnosis best
 - Treatment
 - Reduction of MAwP and PEEP
 - Usually no specific treatment is needed, or possible
 - Analgesia may be helpful/required
- Pneumopericardium
 - Rare, high mortality complication
 - Often associated with hypotension, bradycardia, cyanosis
 - Radiograph reveal heart looking like ball hanging on a string
 - Treatment
 - Emergent needle aspiration or pericardial tube placement
- Systemic air embolism
 - Rare complication in which gas ruptures through into pulmonary veins and fills heart and circulation
 - Almost always rapidly fatal, with no specific treatment possible

Chronic lung disease (CLD) including bronchopulmonary dysplasia (BPD)

- Usually occurs in premature babies exposed to mechanical ventilation
- Often develops in extremely low birthweight (ELBW) infants who require little ventilator support or supplemental oxygen
- Diagnosis based on clinical or laboratory evidence of pulmonary disease, including need for supplemental oxygen) at 28 d (CLD) or at 36 wks corrected gestational age (BPD)
- Signs often seen earlier in ELBW infants at 7–10 d of age
- History of PDA and fluid overload are predisposing factors
- Hypoxemia and/or hypercapnia may be present
- Radiograph shows coarse reticular pattern, cystic structures, streaky densities, and hyperinflation
- Prevention
 - Low ventilation pressures, early course of Vitamin A and caffeine therapy
 - Avoidance excessive baro- or volutrauma early in course
 - Limited fluid intake
 - Preventing complications known to predispose
- Treatment
 - Limit fluid intake
 - Promote growth with adequate caloric intake
 - Low-level ventilator support often for prolonged periods
 - Supplemental oxygen
 - In very severe cases, short courses of corticosteroids may be needed

CARDIOVASCULAR

Cyanosis

- Low PaO₂
 - Congenital heart disease, pulmonary disease, airway obstruction, extrinsic lung compression, CNS disease
- Normal PaO₂
 - Polycythemia
 - Methemoglobinemia
 - Cold stress (the last 3 have a normal)

	Cyanotic CHD	Cyanotic w/CHF
PaO ₂ on 100% O ₂	<50 mm Hg	<150 mm Hg
Congenital heart disease	D-TGA (±IVS) TAPVR truncus arteriosus Ebstein's anomaly Tricuspid atresia Pulmonary atresia with IVS Severe pulmonic stenosis Severe tetralogy of Fallot	Hypoplastic left heart

• Cardiac evaluation

- Physical examination, vital signs (including 4 extremity BPs)
 - Radiograph: heart size, pulmonary vascular markings, major vessels, cardiac and visceral situs, other anomalies
 - Electrocardiogram
 - Axis
 - Frontal plane loop (if suspicion of A-V canal defect or tricuspid atresia)
 - R wave progression
 - Hyperoxia test
 - A "post-ductal" PaO_2 150 mm Hg on FiO_2 = 1.0 is strongly suggestive of intracardiac or ductal R-L shunting due to structural anomaly
 - "Pre" and "post"-ductal PaO₂
 - Useful for distinguishing between intrapulmonary vs. cardiac/PDA shunting
 - Intrapulmonary shunting (e.g., V/Q mismatch), the measurements should be similar
 - Unoxygenated blood shunted R-L across an intracardiac lesion or PDA results in the preductal measurement being higher than the post-ductal (the O₂ Sat will be at least 10% higher)
 - Echocardiography
 - Usual standard that defines anatomy
 - Doppler studies yield flow rates and hence pressure gradients
 - Pressures, cardiac outputs measured this way do not always correlate exactly with catheterization data
 - Catheterization
 - Exactly defines anatomy
 - Sometimes necessary for staging pre-operatively
 - Rarely needed in initial evaluation
 - Used therapeutically in some cases
 - Balloon atrial septostomy
 - Clamshell ASD/VSD closure
 - Umbrella PDA closure in older children

Congestive heart failure (CHF)

- Signs:
 - Hypoxemia is initial sign. Other symptoms: tachypnea, tachycardia, hepatomegaly, inordinate weight gain, cardiomegaly
- Radiograph
 - Cardiomegaly, congested lung fields
- Treatment
 - Oxygen
 - Fluid restriction
 - Furosemide 1 mg/kg IV push or other diuretics
 - Cardiotonics, afterload reduction as needed

Patent ductus arteriosus (PDA)

- Often manifested in 1–3 d old premature infant
- Systolic murmur at upper left sternal border
 - Often silent in ELBW infants

- Bounding or wide pulses
- Active precordium
- CHF, hepatomegaly
- Radiograph
 - Cardiomegaly, pulmonary congestion
- Diagnosis
 - Echocardiography (particularly with Doppler) provides definitive proof of PDA
- Treatment
 - Characterization of hemodynamically significant PDA is unclear, as is benefit of treatment in overall population
 - Fluid restriction
 - Medical therapy: Indomethacin 0.2 mg/kg 1st dose, then 0.1 mg/kg q12h for 24 hrs if <48 hrs. 0.2/0.2/0.2 if 2–7 d; 0.2/0.25/0.25 if >7 d infant
 - Contraindications
 - Renal failure, severe thrombocytopenia, ongoing bleeding, necrotizing, enterocolitis, intraventricular hemmorhage
 - Surgical ligation indicated after failed medical therapy in hemodynamically significant cases
- Blood pressure
 - The normal blood pressure in the premature neonate is not well defined
 - A mean arterial pressure (MAP) >35 mm Hg is considered normal in term babies
 - For premature infants in first few days, normal MAP is considered to be more than the weeks of gestational age + 2
 - ullet Some caregivers believe that a MAP \geq 30 mm Hg is needed to ensure cerebral perfusion independent of gestational age
- Treatment
 - 10 cc/kg of normal saline given over 30 min
 - Blood transfusion if hematocrit is low
 - Vasopressors once fluid balance has been optimized
 - Dopamine at 3–30 mcg/kg/min
 - Dobutamine may be added up to 20 mcg/kg/min but is of questionable benefit
 - Epinephrine 0.1–1.0 mcg/kg/min for severe cases or vasodilation (warm shock)

FLUIDS AND ELECTROLYTES

General facts

- Total fluid per day varies from 40–150 ml/kg/d
- Factors increasing fluid requirements include
 - Lower weight
 - Younger gestational age
 - Immature or injured skin integrity
 - Elevated urine output
 - Low humidity environment
 - Anomalies with surface defects (omphalocele, myelocele, etc.)
- Relatively dilute electrolyte solutions are used in neonates, due to greater insensible water

losses/kg

- Fluid requirements tend to increase in days after birth
- The normal neonate loses weight in the first few days of life, and does not regain birthweight for up to 7 d
- Phototherapy may increase insensible water losses
- Weight loss up to 10% may be normal

Common fluid maintenance regimens in humidified incubator

- Day of life (DOL) #1:
 - Birthweight > 1,200 g: BW: 80 ml/kg/d D10 W
 - Birthweight < 1,200 g: BW: 100 ml/kg/d D10 W
 - Birthweight < 1,000 BW: may require increased intake if losses are increased
 - Add calcium gluconate 200–400 mg/kg/d
 - Premature
 - Depressed babies
 - Infants of diabetic mothers (IDMs)
 - Glucose infusion rate
 - 4–8 mg/kg/min in term babies
 - 6–8 mg/kg/min for prematures
 - Adjust based on measured glucose
 - Monitor electrolytes, but note that initially the baby's serum values are mostly reflective of the mother's. Smaller babies get earlier labs, usually 8–12 hr of age, bigger ones at 24 hrs
- DOL#2: and thereafter
 - 20 ml/kg/d increase unless there is a supervening concern
 - Maximum usually 140 ml/kg/d
 - Na: 2-4 mEq/kg/d
 - K: 2 mEq/kg/d
 - Use chloride salts or acetate if there is metabolic acidosis
 - Calcium as needed
 - Adjust intake to ensure urine output of 2–3 ml/kg/hr
- Renal function
 - Little urine output in first 12–24 hrs is normal if no intake
 - Oliguria is defined as <1 ml/kg/hr in the neonate
 - Treatment
 - IV fluid bolus 10–15 ml/kg normal saline
 - Increased maintenance fluids
 - Assess renal function
 - Ultrasound to rule out anatomic anomaly or obstruction
 - Serum creatinine
 - Assess cardiovascular status

Hypoglycemia (serum glucose <45)

- Definition of hypoglycemia is not well established
- Normal level usually will increase in first several days of life
- Clinical signs
 - Often asymptomatic, jitteriness, tachypnea

- Differential diagnosis
 - Hyperinsulinemic states
 - Infant of diabetic mother, small for gestational age, sepsis, inborn errors of metabolism, birth asphyxia
 - Diminished stores
 - Small for gestational age
 - Inborn errors of metabolism
 - Other
 - Polycythemia/hyperviscosity
- Treatment
 - Monitoring of at-risk infants after birth
 - Increased feeding frequency
 - Adding glucose to feeds
 - Acute management
 - 200 mg/kg glucose IV push = 2 cc/kg D10 W
 - Follow with continuous infusion at 8 mg/kg/min glucose
 - Adjust infusion based on repeat levels

Hyperglycemia

- Causes
 - Excess glucose administration
 - Stress
 - Sepsis
- Clinical presentation
 - Asymptomatic
 - Osmotic diuresis
- Treatment
 - Insulin infusion
 - 0.01–0.05 u/kg/hr
 - Adjust in increments of 0.005–0.01 u/kg/hr
 - Prime IV tubing with infusion before administering

Hypocalcemia (Ca < 7 mg/dl, or use ionized calcium level)

- Causes
 - Asphyxia, prematurity, infant of diabetic mother, hypoparathyroidism, diuretics, alkalosis
- Clinical presentation
 - Jitteriness, apnea
- Treatment:
 - Symptomatic, or the presentation is acute, give Ca gluconate 200 mg/kg IV slowly = 2 cc/kg 10% calcium gluconate
 - Asymptomatic: increase maintenance and monitor
 - Rapid IV infusion of calcium may cause bradycardia

NUTRITION

Goals

- Target weight gain is 10–15 g/kg/d
- Actual weight gained will be lower for smaller babies
- Length gain: 0.8–1.2 cm/wk
- Head circumference growth: 0.5–0.8 cm/wk
- Human milk is best substrate
 - For premature infants, milk usually requires supplementation in calories, protein, minerals

Requirements for growth

• Calories: 110–150 kcal/kg/d

• Protein: 3.5–4 g/kg/d

• Fat: 2–3 g/kg/d

Method of feeding

- Enteral feeds are optimal
 - Immature or compromised infants may initially feed via gavage tube, later PO
 - Bolus feeds every 3–4 hrs are the goal
 - In some infants (usually <1,000 g) continuous feeds are necessary
 - Feedings must initially be advanced slowly over days to ensure tolerance
 - In babies <1,000 g, feeds start as "gut priming"
 - Use human milk
 - Feed 0.5 ml every 4 hrs for 3 d
 - Then begin feeding advance as below
- Start with 20 cal/ounce feeds
 - Human milk is presumed to be 20 cal/ounce
 - When on full volume, increase feeding density as needed to promote growth
 - Formulas made to increase density
 - Human milk fortified to caloric density
 - Most babies <1,500 g will need increased density
- Begin iron supplementation when on full feedings (see Table below)
- Remain vigilant for feeding intolerance or signs of gastrointestinal disease
 - If present, hold feedings and evaluate

Suggested Rates for Initiation and Advancement of Nutritive Feedings				
Birthweight (g)	Initial Rate (ml/kg/d)	Volume Increases (ml/kg every 12 hrs)		
<1,000	10	10		
1,001-1,250	10-20	10		
1,251-1,500	20–30	10-15		
1,501-1,800	30	15		
1,801-2,500	30-40	15-20		

Total parenteral nutrition (TPN)

- Used instead of enteral feedings
 - Infant is ill
 - During feeding advance to allow adequate nutrition without overloading gut
 - Should be started as soon as prolonged IV nutrition is anticipated
 - Begin right after birth for babies <1,200 g

- Composition
 - Begin with total ml/kg allocated to TPN, order lipid infusion first
 - (Intravenous fat emulsion = 20% intralipid)
 - Weight < 1,000 g start at 0.5 g/kg and advance by 0.5 g/kg/d to maximum of 3 g/kg/d
 - Weight > 1,000 g start at 1 g/kg/d and advance by 1 g/kg to maximum of 3 g/kg/d
 - Determine amino acid concentration
 - Amino Acid solution = TrophAmine
 - Start at 2 g/kg/d and advance by 0.5–1 g/kg to maximum of 3–3.5 g/kg/d
 - Determine glucose infusion rate
 - Begin with 4–6 mg glucose/kg/min
 - Advance by 1–2 mg glucose/kg/min to maximum 11–12 mg glucose/kg/min
- TPN also contains vitamin and trace minerals
 - Measure serum electrolytes, lipids, ALT, AST weekly
 - Urine glucose should be checked if there is a suggestion of hyperglycemia
- Parenteral nutrition can begin at admission, especially for babies <1,250 g, using a standard PN that has no added electrolytes or vitamin (to increase shelf life)

Neurology

Intraventricular-periventricular hemorrhage (IVH)

- Common problem, especially in infants <32 wks gestation
 - Most are mild
 - Exact etiology unknown
 - May be associated with shifts in blood pressure
 - May follow large pneumothorax
 - Associated with more severe overall illness
- Clinical signs
 - Often silent
 - Severe cases: signs of acute blood loss, seizures, change in fontanel
- Diagnosis
 - Head ultrasound examination
 - Infants <32 wks screened
 - Day 1–2 for most immature babies
 - Day 7–10 for stable babies
 - Repeat at day 10, 30 and q30d
- Treatment
 - Primarily supportive, prevention is important
 - Post-hemorrhagic hydrocephalus may occur in severe cases
 - May require repetitive lumbar punctures to relieve pressure
 - May require shunt for long term treatment
- Prognosis
 - Overall positive in milder cases
 - Guarded with more severe cases
 - Intraparenchymal hemorrhage, early neurologic signs

Seizures

- Distinguish from jitteriness
 - Seizures do not extinguish with holding
- Often subtle or incomplete in neonates
 - Lip smacking
 - Abnormal gaze
- Etiology
 - Hypoxic ischemic injury
 - Usually tonic
 - Occur 12–24 hrs after injury in global injury
 - May occur early with acute brief injury
 - IVH (premature)
 - Usually tonic
 - Trauma/CNS hemorrhage
 - Stroke
 - Usually unilateral clonic
 - Infection/meningitis
 - CNS malformations
 - Vascular malformation
 - Metabolic diseases
 - Organic acidemia, urea cycle defect
 - Electrolyte abnormalities
 - Hypocalcemia, hyponatremia
 - Hypoglycemia
 - Pyridoxine deficiency
- Evaluation
 - Head ultrasound, MRI when available, CT scan rarely needed, poses long term risk, CBC with differential, arterial blood gases, electrolytes, glucose, calcium, ammonia
- Treatment
 - Phenobarbital
 - Load w/10-20 mg/kg
 - Maintain with 2–5 mg/kg/d
 - Therapeutic level = 20–40 mcg/ml
 - Fosphenytoin
 - Load 10 mg/kg
 - Infrequently used
 - Lorazepam

Apnea of prematurity

- Common at <32 wks
- May occur up to 35–36 wks
- Typical onset day 2–3
- Diagnosis of exclusion
- Differential diagnosis
 - Atelectasis, sepsis, hypoglycemia, hypocalcemia, IVH

- Seizures
 - Rare as sole presentation of seizures
- Opioids
- Electrolyte abnormalities
- Airway obstruction
- Vagal stimuli (indwelling feeding tube, moving ET tube)
- Evaluation
 - CBC w/diff, PLTS, glucose level, electrolytes, calcium, chest radiograph, head ultrasound screen
- Treatment
 - Caffeine
 - Load with 20 mg/kg IV
 - Maintenance 5–10 mg/kg q24h
 - No levels need to be drawn
 - Oxygen supplementation
 - Nasal cannula
 - CPAP or high flow nasal cannula
 - Intubation (rarely)

Periodic breathing

- Up to 10 sec of apnea followed by normal respiration
- Occurs in many preterm babies
- Low frequency after 36 wks gestational age
- No specific therapy

Agitation

- Sedation should be used with caution in newborns
- Term infants
 - Phenobarbital
 - Benzodiazepines (diazepam, lorazepam)
 - Lorazepam may cause myoclonus in premature infants
 - Morphine or fentanyl are commonly used, particularity if there is a component of pain
 - Monitor for respiratory depression

Pain

- Babies feel pain, at least after 22–24 wks of gestation
- Oral sucrose can provide pain relief in mild instances
- Ensure adequate analgesia for noxious, or painful procedures, or intervention
- Assessment scales are used to guide therapy

GASTROENTEROLOGY

Feeding intolerance

- Common problem in premature infants
- Often occurs during feeding advance
- Baby is otherwise apparently normal

- Clinical signs
 - Increased gastric residuals, abdominal distention, distended bowel loops, no signs of ileus, difficult to initially distinguish from NEC
- Evaluation
 - Hold feedings
 - Radiograph may be helpful in ruling out pathologic condition
 - Observation for several hours
 - Sometimes progresses to more extensive evaluation to rule out NEC

Necrotizing enterocolitis (NEC)

- Idiopathic intestinal necrosis
 - Associated with prematurity
 - Presumed to be the result of bacterial action on an already compromised bowel
 - Most common in terminal ileum and ascending colon
 - Most suspected cases ultimately not confirmed
- Clinical signs
 - Abdominal distention, tenderness, hematochezia, gastric aspirates before feedings, ileus, metabolic acidosis
 - Non-specific signs
 - Apnea and bradycardia, shock
- Diagnosis
 - Radiographic
 - Pneumointestinalis gas bubbles in bowel walls
 - Air in biliary tree, pneumoperitoneum
 - Surgical
 - Peritonitis, bowel necrosis, perforation
- Differential diagnosis
 - Sepsis
 - Intra-abdominal catastrophes (midgut volvulus, etc.)
 - Infectious enterocolitis (rare)
 - Metabolic disease
 - Feeding intolerance
 - Allergic colitis (see below)
- Evaluation
 - Should be done whenever there is heightened suspicion
 - Feedings should be held
 - Physical examination
 - KUB and left lateral decubitus. Repeat q6–8h as long as suspicion remains
 - CBC/diff, blood cultures and electrolytes
 - Sepsis evaluation
 - ABG if indicated
 - Surgical consultation if suspicion high or diagnosis confirmed
- Treatment confirmed or clinically suspicious cases
 - The majority of cases are treated without need for surgery
 - Stop all enteral feedings for 14 d

- Replogle tube for GI decompression
- Broad spectrum antibiotics
- Include coverage for potential anaerobic organisms
- Repeat radiographs until stable
- If perforation or clinical deterioration occurs surgery is indicated
- There is risk of intestinal stricture presenting weeks after acute course

HEMATOLOGY

Mean hematocrit at birth is 51% at term, lower in premature infants Circulating blood volume is approximately 80 ml/kg

Anemia (Hct < 30)

- Cause
 - Blood loss
 - Feto-maternal, phlebotomy, hemorrhage
 - Hemolytic diseases
 - Immune mediated
 - Blood type incompatibilities
 - Non-immune
 - Red cell defects (spherocytosis, etc.), enzyme deficiencies, G6PD, pyruvate kinase
 - Congenital infections
 - CMV, rubella, parvovirus 19
 - Anemia of prematurity
 - Low reticulocytosis, phlebotomy, rapid growth
- Evaluation
 - Smear, reticulocyte count, central hematocrit, type and coombs
 - Kleihauer/Betke on mother
 - Head ultrasound or other studies to locate bleeding may be needed
- Treatment
 - DOL#1-3: Transfuse for Hct < 35-40 if
 - Hypotensive
 - Moderate or severe respiratory disease
 - DOL > 3: transfuse if Hct < 35 if
 - Sepsis, oxygen dependent, still requires ventilator support, tachycardic, tachypneic without other cause, poor weight gain despite adequate intake

Polycythemia

- Hematocrit >65 with symptoms, >70 without
- Confirm with central hematocrit
- Higher risk in
 - SGA, IDM, recipient twin in twin–twin transfusion
- Clinical signs
 - Hypoglycemia, hypocalcemia
 - Abnormal neurologic examination

- Treatment
 - Partial exchange transfusion to reduce Hct to 50–55
 - May reverse minor symptoms, but will not change neurologic outcome

Hemorrhagic disease of the newborn

- Coagulopathy and hemorrhage due to low Vitamin K levels
- Usually presents with severe and life threatening GI hemorrhage at 3 d
- May present at 1–2 wks, usually with acute CNS hemorrhage
- Treatment
 - Preventative, 1 mg Vitamin K IM at birth

Hyperbilirubine mia

- Principles
 - Physiologic jaundice is common in newborns
 - Accelerated red cell destruction
 - Immature excretion pathways
 - Normally transient
 - Peaks on day 3–5, may decline slowly over weeks
 - Most bilirubin is bound to albumin in serum
 - Risk of bilirubin neurotoxicity exists from unconjugated bilirubin
 - Bilirubin not bound to albumin
 - Abnormal or injured blood brain barrier
 - Pathologic causes can result in dangerously high levels
 - Hemolysis, enzyme deficiencies, defects in conjugation and excretion, metabolic disorders, hypothyroidism
 - Markedly elevated levels are dangerous
 - Otherwise healthy term infants are at low risk with peak levels <22–25 mg/dl
 - Danger level in preterm not well established
 - Often considered to be level equal to 1 percent of birthweight (e.g., 1,400 g BW danger level is considered to be 14)
 - Danger increased at lower levels when hemolysis or illness present
- Monitoring
 - All term and late preterm infants should have screening level at 24–36 hrs
 - AAP guidelines suggest repeat monitoring, when to start therapy (*Pediatrics*. 2004;114:297–316)
 - Premature infants should have screening level at 12-24 hrs
 - Base decisions on repeat monitoring on level, rate of rise, postnatal age
 - Goal: prevent serum concentration from exceeding determined danger level
 - Unusually high levels should prompt evaluation for pathologic cause
 - Type and Coombs, CBC, reticulocyte count, urine reducing substances, thyroid hormone levels
- Treatment
 - Ensure normal hydration status
 - Phototherapy
 - Begin at levels about ½ of danger level
 - Efficacy depends on:
 - Intensity, wavelength of light (blue), exposed surface area, duration of therapy
 - Stop when level has dropped below trigger level

- Level normally rebounds 0.5–1.0 mg/dl within 12–18 hrs
- Exchange transfusion
 - Requires large IV or UVC
 - May be done with arterial and venous access
 - A volume twice the circulating blood volume is exchanged in aliquots
 - Level usually decreases by 50% immediately after procedure

INFECTIOUS DISEASES

Evaluation of the asymptomatic infant at risk for sepsis and meningitis

- Newly born infants at risk for sepsis are initially asymptomatic
- Evaluation done on the basis of historical factors
 - Known maternal GBS colonization, without treatment during labor (4 hrs)
 - Maternal fever >100.4°F (38.5°C)
 - Maternal chorioamnionitis
 - Prematurity <35 wks
 - Previous child with GBS disease much higher risk
- White cell count immediately after birth of minimal value better obtained at 6–12 hrs
- Abnormal white count with elevated immature: total neutrophil count raises concern
- Therapy
 - Indicated empirically for maternal fever >101°F, maternal chorioamnionitis, abnormal cell count, symptoms
 - Broad spectrum antibiotics
 - Ampicillin, gentamicin
 - Primary organisms are GBS, E. Coli, rarely Listeria
 - Alter choices based on local flora

Bacterial sepsis

- A concern in any infant with consistent signs of:
 - Respiratory distress, hemodynamic instability, abnormal neurologic findings, temperature instability, other signs without apparent cause
- Evaluation
 - CBC differential, blood cultures, CSF examination
 - May delay until decision to treat for full course

CSF Fi	ndings in Non-men	ingitic High-r	isk Infants	
	Preterm	Mean	Term	Mean
WBC (±SD)	0-25	9	0-22	8.2
% PMN	57		61	
Protein (range)	65-150	115	20-170	90
Glucose (range)	22-63	50	34-119	52

CSF in the newborn may normally have 600-900 RBC/mm³

- Therapy
 - Warranted when concern arises

- Can be stopped after 48 hrs if evaluation negative
- Likely organisms change with postnatal age
 - First several days perinatal acquisition likely
 - Ampicillin/gentamicin as above
 - Late in first week to 3 wks of age
 - Add coverage for coagulase *staphylococcus* with indwelling lines/appliances
 - Consider coverage for Staphylococcus aureus, local flora

Hepatitis B prophylaxis

- First dose of hepatitis B vaccine
 - Term infants in first day
 - Premature infants given at 2 kg weight
 - If mother is known HbsAg (+), the baby is given hepatitis B immune globulin (HBIG) 0.5 ml in the first 12 hrs of life, along with the vaccine

Ophthalmia neonatorum (neonatal conjunctivitis)

- Microbial causes include Neisseria gonorrhoeae, chlamydia, staphylococcus
- All babies should receive eye prophylaxis at birth (erythromycin ointment)

Congenital infections

- Cytomegalovirus (CMV), rubella, other viruses
- Clinical signs
 - Petechiae, hepatosplenomegaly, jaundice (conjugated), microcephaly, SGA, chorioretinitis, intracranial calcifications
- Later onset cases of CMV may result from transmission via breast milk

Human immunodeficiency virus (HIV)

- Most infected children are asymptomatic in the neonatal period
- Lab diagnosis is difficult because of persistence of maternal anti-HIV antibody
- Viral culture and antigen p24 detection are useful
- Antiretroviral therapy begun at birth for at-risk babies

SYNDROMES AND ASSOCIATIONS

- VATER (VACTERL) Vertebral anomalies anal atresia cardiac defects (VSD or other) TE (tracheo-esophageal) fistula renal dysplasia limb deformities (radial and other digital abnormalities)
- **Beckwith–Wiedemann Syndrome.** Macrosomia. Large muscle mass. Macrosomia, hypoglycemia macroglossia. May present difficulties eating or breathing visceromegaly, including pancreatic hyperplasia with excess islet cells (hence hypoglycemia)Omphalocele and other abdominal defects.
- **Trisomy 21** (Down syndrome). 1:1,000 births hypotonia, brachycephaly, mongoloid slant to eyes, epicanthal folds, protruding tongue, redundant skin on neck, small ears □3 cm) Simian crease, short metacarpals, 5th finger clinodactyly. Increased space between first and second toes A V canal, VSD, PDA
- Trisomy 18 (Edward syndrome). 1:3,000 births. Growth deficiency, prominent occiput, low set

- ears, short palpebral fissures, clenched hand, overlapping index/3d, 4th/5th fingers, nail hypoplasia, short hallux. Rocker bottom feet. Short sternum, VSD, ASD, PDA umbilical hernia
- **Trisomy 13** (Patau syndrome). 1:6,000 births holoprosencephaly, microcephaly, sloping forehead, microphthalmia, scalp defect, cleft lip/palate, abnormal/low set ears. Simian crease, polydactyly, PDA, VSD, and dextroposition. Single umbilical artery

	Antibioti	ics: Neonatal D	osing		
Antibiotic	Dose (per dose)	Interval by Po	ostconceptual	Age or Weight	
		<30 wks	30-35 wks	36-42 wks	
Ampicillin	50–150 mg/kg	q12h q8h > 28 d	q12h q8h > 14 d	q12h q8h > 7 d	
Gentamicin	3 mg/kg 4 mg/kg	<35 wks q24h		≥35 wks q24h	
Cefotaxime	50 mg/kg	≤7 d q12h qh8 > 28 d	>7 d q12h q8h > 14 d	q12h q8h > 7 d	
Clindamycin	7.5 mg/kg	≤29 wks q12h q6h > 1 mo	≥29 wks q8h	>29 wks	
Amphotericin B	0.25-0.5 initial	q24-48h 0.5-1.0 mg/kg	<37 wks	≥38 wks	
	Term		Preterm		
AZT	2 mg/kg PO q6h 1.3 mg/kg IV			/kg/dose PO q12h g/dose PO q8h	
Acyclovir	20 mg/kg q8h for 14	4–21 d	20 mg/kg q8h for 14-21 d		
Vancomycin	≤7d < 1.2 kg 1.2–2 kg >2 kg >7 d ≤ 1.2 kg 1.2–2 kg >2 kg		15 mg/kg IV q24h 10 mg/kg IV q2h 15 mg/kg IV q2h 15 mg/kg IV q24h 15 mg/kg IV q12h		

PEDIATRIC INTENSIVE CARE

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KEY PRINCIPLES FOR PEDIATRIC CRITICAL CARE

- Normal physiology, anatomy and vital signs all change with age
- Dosing of drugs, fluids, electrolytes is typically based on weight or BSA

	Normal Physiologic Values					
Age	Weight (kg)	Systolic Blood Pressure	Heart Rate	Respiratory Rate	ETT Size	ETT Depth
Newborn	3.5	60	100-180	30-40	3-3.5	9
to 6 mo	6	70	100-160		3.5-4.0	11
1	10	72			4	12
2	12	74	80-110	25-32	4.5	13
3	14	76			4.5	14
4	16	78	70-110		5	
5	18	80	65-110	22-28	5	15
6	20	82	18.77 12.34.5		5.5	
7	22	84			5.5	16
8	24	86			6	
9	26	88			6	19
10	28	90-120		20-24	6.5	

SBP, systolic blood pressure; ETT, endotracheal tube.

Quick Calculations

- Weight (kg) = 8 + 2 (age in years)
- Body surface area (BSA) (m²) = [ht(cm) × wt(kg)/3,600]1^{/2}; 1 in. = 2.54 cm; 1 kg = 2.2 lbs
- SBP = 70 + 2 (age in years)
- ETT (uncuffed) = 4 + (age in years/4)
- ETT (cuffed) = 3 + (age in years/4)
- ETT depth $\approx 3 \times (ETT diameter)$
- Maintenance fluids
 - 1-10 kg = 4 ml/kg/hr
 - 11-20 kg = above plus 2 ml/kg/hr
 - >20 kg = above plus 1 ml/kg/hr
 - That is, $18 \text{ kg} = (4 \times 10 \text{ kg}) + (2 \times 8 \text{ kg}) = 56 \text{ ml/hr}$
- Fluid bolus = 20 ml/kg normal saline or LR

Common Problems Encountered in Pediatric ICU

Shock

- Tissue perfusion inadequate to meet metabolic needs (cardiac output = stroke volume × heart rate)
 - Phases of shock:

- Compensated shock: tachycardia, vasoconstriction to maintain cardiac output and blood pressure
- Decompensated shock: hypotension AND weak central pulses, decreased urine output (UOP), altered mental status, metabolic acidosis, tachypnea
- Types of shock:
 - Hypovolemic
 - Most common cause in pediatrics
 - Diminished intravascular volume; decreased preload
 - Dehydration, sepsis, blood loss, diarrhea, vomiting, third spacing of fluids
 - Signs of dehydration: tachycardia, decreased UOP, tachypnea, decreased level of consciousness
 - Management:
 - Assure adequate airway and ventilation
 - Intravascular volume repletion: isotonic crystalloids 10–20 ml/kg; assess and repeat fluid administration if required
 - Antibiotics (Abx) as soon as possible if suspected infection
 - Cardiogenic
 - Various etiologies including myocarditis, cardiomyopathy, tamponade, arrhythmias, congenital heart disease, toxins
 - Diagnostic approaches: EKG, CXR, echocardiogram, check electrolytes

Management:

- Treat arrhythmia; inotropic support (dobutamine, dopamine, epinephrine)
- Neurogenic
 - Hypotension with bradycardia. Weakness and flaccidity
 - Diagnostic approaches: C-spine films, CT/MRI
 - Management:
 - Intravascular volume expansion, inotropes, consider high-dose steroids
- Anaphylactic
 - Tachycardia, tachypnea, bronchospasm, flushing, hypotension, urticaria
 - Management:
 - Diphenhydramine, corticosteroids, epinephrine, H₂ blockers

Sepsis (also see Chapter 10)

- Systemic inflammatory response syndrome (SIRS)/septic shock
 - At least 2 of the following, one of which must be altered T° or WBC
 - Core $T^{\circ} > 38.5$ or < 36
 - Tachycardia (HR > 2 SD above nl for age) controlled for external stimulus, pharmacologic stimulus, painful stimulus
 - Mean respiratory rate >2 SD above normal for age
 - Elevated or depressed WBC or >10% bands
- Sepsis: symptoms of SIRS in the presence of proven or suspected infection
- Severe sepsis: sepsis with evidence of end-organ dysfunction
- Septic shock: sepsis and cardiovascular organ dysfunction (sustained hypotension despite sufficient intravascular volume resuscitation)

Management:

• Includes early and aggressive fluid resuscitation (20 ml/kg aliquots readily up to 60 ml/kg total if necessary), early institution of broad spectrum antibiotics; vasopressor and/or inotropic support if fluid resuscitation not sufficient

Diabetic ketoacidosis (DKA)

- Serum glucose > 200 mg/dl with ketonemia/ketonuria and pH < 7.30; accompanied by electrolyte abnormalities and hypovolemia
- pH reflective of insulin deficiency; hyperglycemia reflective of hydration status
- Cerebral edema #1 cause of mortality. Incidence of DKA: 1%, mortality: 20%, permanent neurologic deficit: 25% associated with resuscitation of >4 1/m²/24°
- Avoid overly vigorous correction of dehydration and hyperglycemia
- Artifactual hyponatremia, total body hypokalemia with initial normal/elevated serum level K+, hypophosphatemia
- Management: aimed at correction of hyperglycemia, acidosis, electrolyte deficits, and dehydration
- Electrolyte and fluid requirements vary greatly
- Guide to fluid resuscitation: initial isotonic fluid bolus (10 ml/kg) to correct impending shock. Correct remaining deficit over 36–48 hr. Use 0.45% normal saline (NS). Add K+ after first void (Kphos + Kacetate/KCl, avoid phos if Ca is low). Consider NS if Na remains low after glucose falls or if concerns about cerebral edema
- Insulin 0.1 U/kg/hr in NS. Goal: decrease serum glucose 50–100 mg/dl/hr
- When blood glucose (BG) is between 250–300 or if it falls >100 mg/dl/hr add D5
- Avoid bicarbonate
- Monitor: BG q1h; VBG, electrolytes, Ca, phos q2h until stable then q4–6h; urine ketones/glc. Consider EKG if electrolyte abnormalities
- When pH > 7.3 and BG < 300, add nutrition and change to SQ insulin

Status asthmaticus

- Accessory muscles, dyspnea, wheezing, pulsus paradoxus
- Monitor O₂ sats and oxygenation, and peak expiratory flow
- Management:
- Supplemental O₂

- Fluids: correct dehydration; avoid overhydration
- Corticosteroids: methylprednisolone (limited mineralocorticoid) 2 mg/kg; then 0.5–1 mg/kg q6–12h (max 120 mg). Oral prednisone in less severe cases
- Inhaled beta agonists: continuous nebulized albuterol 0.15–0.5 mg/kg/hr = 10–20 mg/hr. Sinus tachycardia common but rarely problematic
- IV beta agonists: terbutaline 10 mcg/kg load over 10 min; then 0.1–10 mcg/kg/min Monitor for hypokalemia and supraventricular tachycardia (SVT) (avoid adenosine if SVT as can worsen bronchospasm). ECG, CK/troponin, electrolytes q12h
 - Consider:
 - Anticholinergic: ipratropium 125–500 mcg neb/4–8 puffs MDI q4–6h
 - Magnesium sulfate 40 mg/kg/dose over 30 min, consider fluid bolus prior to administration to prevent hypotension
 - Heliox decreases airflow resistance in small airways, cannot be used with hypoxemic patients given low FiO₂ with 70/30 or 80/20 mixture
 - Antibiotics: usually viral or allergic provocation but might be bacterial (esp. mycoplasma)
 - Non-invasive ventilation
 - Mechanical ventilation: <1%. Refractory hypoxemia, hypercarbia, acidosis not responsive to pharmacotherapy. Severely depressed mental status
 - Ventilator management: avoid hyperinflation and air trapping. Disease of expiratory obstruction. Low positive end expiratory pressure (PEEP), long expiratory time, slow rate. Adjust MV to keep arterial pH > 7.25
 - Sedatives: ketamine continuous infusion 1st choice 1 mg/kg/hr (side effect: increased secretions)
 - Muscle relaxants: vecuronium 0.1 mg/kg/hr

Bronchiolitis

- Bronchiolar inflammation with obstruction of small airways
- Peak incidence 12 mo (3 mo-3 yrs)
- High risk for complications: premature and ex-premature, congenital heart disease, bronchopulmonary dysplasia, immunodeficient, cystic fibrosis, age <3 mo
- Respiratory syncytial virus (RSV) most frequent cause

Management:

- Hydration
- Oxygenation: pulmonary toilet; nasal prongs; continuous positive airway pressure (CPAP); mechanical ventilation
- β_2 agonists trial: discontinue if no change or worsening
- Consider racemic epinephrine
- Treat secondary bacterial infection
- Consider steroids (controversial) inhaled/systemic

Acute respiratory distress syndrome (ARDS)/acute lung injury (ALI) (Chapter 5)

- Patients with pneumonia, sepsis, bacteremia, trauma, burns, pancreatitis, aspiration pneumonitis, fat embolism, near drowning, massive blood transfusion
- Mortality 20%–75%; 1%–4% of PICU admissions
- Acute non-cardiogenic pulmonary edema with bilateral infiltrates
- ARDS $P_aO_2/F_iO_2 < 200$
- ALI P_aO_2/F_iO_2 200–300

Management:

- Early arterial access to evaluate and follow disease (P_aO₂/F_iO₂ and oxygenation index (OI))
- CPAP/bilevel positive airway pressure (BiPAP) for alveolar recruitment. PPV for impending respiratory failure
- Titrate PEEP to achieve $F_iO_2 \le 0.6\%$ and S_pO_2 88%–95%
- Limit tidal volumes (Vt) to 6 cc/kg and alveolar pressure to <30 cm H_2O
- Permissive hypercapnia unless contraindicated
- Transition to high frequency oscillatory ventilation (HFOV) if high inflation pressures required
- Consider prone positioning
- Provide adequate sedation and analgesia, consider neuromuscular blockade
- Early nutritional optimization
- Optimize hemodynamics. Maintain euvolemia. Consider renal replacement therapy for persistent hypervolemia/oliguria despite diuretics
- Extracorporeal membrane oxygenation (ECMO) if prior measures fail

Acute chest syndrome

- Patients with sickle cell disease
- New or rapidly progressive infiltrate on CXR, fever, cough, chest pain (pleuritic), tachypnea, hypoxemia; mortality 25%. Can progress to severe ALI or ARDS
- Usually provoked by infection and/or pulmonary vaso-occlusion
- Diagnostic tests: CBC, CXR, retic, ABG, type and screen, blood/resp cultures. Calculate A–a gradient

Management:

- Generous hydration with guided restraint based on atrial filling pressures, renal function, cardiovascular status
- Supplemental O_2 . Goal $P_aO_2 > 80-100$; $S_aO_2 > 95\%$
- Incentive spirometry and ambulation: decrease atelectasis and V/Q mismatch
- Pulmonary toilet
- Consider albuterol therapy
- Analgesia: opioid based, titrate. Monitor RR/effort. Consider epidural analgesia.
- Consider CPAP, BIPAP, Mech ventilation
- Vent: minimize plateau pressure and Vt. Adjust PEEP to maximize compliance
- Broad spectrum Abx. Send cultures (including respiratory)
- Transfusion of packed RBCs: decrease amount of sickled hemoglobin (HgbS). Increases O₂ carrying capacity. Avoid hyperviscosity. Goal Hb > 10 gm/dl

- Partial exchange transfusion for severe or rapidly progressive disease
- Consider inhaled nitric oxide (iNO), ECMO in severe cases

Tumor lysis syndrome (TLS)

- Patients with acute leukemia, high-grade non-Hodgkin lymphoma (Burkitt's lymphoma), less commonly in solid tumors (neuroblastoma, hepatoblastoma)
- Metabolic abnormality due to rapid lysis of tumor cells
- Usually 12–72° after initiation of chemotherapy (steroids, hormones, radiation might also trigger)
- High risk includes Burkitt's lymphoma/leukemia, ALL
- Characterized by elevated K+, phos, and uric acid. Low Ca++; acidosis

Management:

- Focused on hydration and alkalinization of urine (routine alkalinization controversial due to increased risk of calcium and phosphate precipitation)
 - D5 0.25% NS + 60–100 mEq NaHCO₃/1 @ 2–4x maintenance
 - Keep urine pH 7-7.5 and urine specific gravity 1.010
 - Allopurinol: 10 mg/kg/d 24–48 hrs before initiation of chemotherapy
 - Urate oxidase: 0.15-0.2 mg/kg qd \times 5 d
 - Restrict K+ and phos. Replace Ca only if symptomatic
 - Follow K+, Ca, phos, uric acid

Syndrome of inappropriate secretion of antidiuretic hormone (SIADH)

- Patients with pneumonia, CNS disorders, cirrhosis, congestive heart failure, nephrotic syndrome, taking certain medications
- Excessive antidiuretic hormone (ADH) secretion
- Elevated total body water (TBW), hyponatremia, low serum osmolality (<280 mOsm/l), high urine osmolality (>500 mOsm/l)
- If severe hyponatremia or seizures occur, correct Na rapidly to 120 mEq/l (use 3% NS 1–2 ml/kg aliquots or consider infusion); then 0.5 mEq/l/hr to avoid central pontine myelinolysis

Cerebral salt wasting (CSW)

- Patients with brain injury or brain tumor
- Possibly due to abnormal secretion of natriuretic peptides
- Diminished TBW, low serum Na, elevated UOP, elevated U_{Na}

Management:

- Directed at replacing fluid and Na deficit
- Consider fludrocortisone 0.2–0.4 mg/kg/d

Central Diabetes Insipidus (DI)

- Patients with CNS disease/trauma/surgery
- Impaired ability to concentrate urine due to lack of ADH
- Elevated Na, elevated serum osmolality (>300 mOsm/l), low urine osmolality, low urine specific gravity (<1.005), elevated UOP (>4 ml/kg/hr)

Management:

• Directed at replacing deficits and hormone replacement

- Treat shock; then give maintenance fluid + deficit + ongoing losses
- Correct Na slowly over 48 hrs
- Vasopressin (AVP) 0.5 mU/kg/hr (max 10 mU/kg/hr), titrate to UOP < 2 ml/kg/hr
- Monitor UOP, Na, UOsm

		d Laboratory Results of Inappropriate ADI Salt Wasting	
	DI (central)	SIADH	csw
TBW	Low	High	Low
UOP (cc/kg/hr)	>2-4	<0.5	>2-4
Serum Na	145-155	120-130	120-130
Serum Osm	>300 mOsm/l	<280 mOsm/l	Low
Urine Osm	Low	>500 mOsm/l	High
Urine specific gravity	<1.001	>1.025	<1.005

DI, diabetes insipidus; SIADH, syndrome of inappropriate antidiuretic hormone secretion; CSW, cerebral salt wasting; TBW, total body water; UOP, urine output.

Status Epilepticus (see Chapter 21)

- Consider high-dose Abx, acyclovir
- Generalized convulsive status (GCSE), focal motor, myoclonic
 - First line: lorazepam
 - Second line: fosphenytoin (valproate as well for myoclonic)
- Neonatal status epilepticus (see Table for drug dosing on page 32-8)
 - First line: phenobarbital
 - Second line: fosphenytoin, lorazepam
- Rule out complex febrile seizure
- Consider continuous EEG monitoring

Burn (see Chapter 17)

Trauma

- Leading cause of death in children >1 yr
- Glasgow Coma Score (GCS) was modified for early developmental stages
- Hypothermia, greater risk due to large surface area to mass ratio
- Higher incidence of head trauma given large head to body ratio
- May have little external evidence of internal injury
- Type of trauma related to age
 - Infants: non-accidental, home injury
 - 1–5 yrs: falls
 - Elementary school age: bicycle or car vs. pedestrian
 - Adolescent: motor vehicle crash, violent crime

Management:

- Treat ABCs first
- O₂, volume, blood often more important in resuscitation than medication
- Vascular access can be more challenging than in adults. Consider intraosseous access if no venous access and patient critical. Many resuscitation drugs can be given endotracheally: lidocaine, epinephrine, atropine, naloxone (LEAN)
- Optimize nutritional state

Head injury

- High mortality. Diffuse axonal injury more common in pediatrics (clinical symptoms often out of proportion with radiologic findings). Skull fracture more common than in adults
- Management goals: rapidly treat intracranial hypertension (mannitol, hypertonic saline, consider hyperventilation acutely, CSF drainage, consider barbiturate therapy, head positioning), assure adequate oxygenation, maintain cerebral perfusion pressure (CPP) (avoid hypotension, treat elevated intracranial pressure (ICP)), normothermia. Treat/prevent hypoxia, pain, fever, hypercarbia, seizure, hypo/hyperglycemia
- Neurologic, developmental, and neuropsychiatric sequelae might not be apparent until years later

Spinal cord injury and vertebral injury:

- Often difficult to diagnose radiographically
- Often unique injury patterns due to developmental transition and/or pediatric disease/syndromes
- Spinal immobilization if any concern. Maintain adequate perfusion and oxygenation
- High index of suspicion. Timely diagnosis and treatment
- Spinal cord injury without radiologic abnormality (SCIWORA). Pediatric spinal column more elastic than spinal cord. Obtain CT/MRI, proper immobilization, neurosurgical evaluation

Thoracic injury

- Second to head trauma in mortality
- Compliant mediastinum. Injury on one side can affect other
- Pulmonary contusion: might not be seen on initial X-rays. Can progress to ARDS

Abdominal injury

- Insert Foley, NG tube early
- Serial exams often needed to assist with diagnostics

- Spleen: most common intra-abdominal organ injured. Usually managed non-operatively unless patient hemodynamically unstable and/or losing significant blood volume. Splenectomy increases lifetime risk of sepsis
- Liver: second most common intra-abdominal organ injured. Also typically managed nonoperatively if patient can be stabilized hemodynamically
- Pancreas: most common cause of pediatric pancreatitis. Usually due to direct blow to abdomen. At risk for pseudocyst. Bowel rest, TPN, drainage of fluid, pancreatectomy for ductal injuries with splenic preservation if possible
- Kidney: third most common. Bed rest, monitor hematuria. Majority managed non-operatively
- Bowel: duodenal hematoma. Can lead to obstruction. Usually managed non-operatively (NPO, gastric decompression, TPN). Bowel perforation less common than adults. Peritoneal signs develop more slowly
- GU: bladder and urethral injuries, high index of suspicion with pelvic fractures

Orthopedic injury

- Growth plates can make radiologic diagnosis more challenging
- Consult orthopedics/vascular, esp. if neurologic or vascular compromise

Non-accidental Trauma (NAT)

- Always consider the possibility. Perform a thorough history and physical examination. History often inconsistent with injuries (e.g., femur fracture from a short fall)
- Perineal injuries, shaken baby signs (subdural hematomas, retinal hemorrhages), long bone fractures, multiple fractures of different age, burns, unusual bruising, repeated trauma
- If suspected, thorough work up and child protective services/police involvement required
- Full skeletal survey in children <2 yrs. Ophthalmology evaluation for retinal hemorrhages

Pediatric pain management

- Tailor therapy to individual; multidisciplinary approach
- Pediatric differences: cognitive ability, communicative style, respiratory mechanics and airway anatomy, pharmacologic metabolism
- Self-reporting, most reliable means of assessing pain. Pain scales based on age.
 - Wong–Baker (FACES) (age 5–6) (see Chapter 8)
 - Number scale 1-10 (age >7)
- Pharmacologic modalities: (see page 32-8 for typical dosing)
 - NSAIDs: treat pain, fever, inflammation. Side effects include GI irritation, plt dysfunction, ARF, bronchospasm, closure of patent ductus arteriosus. Aspirin contraindicated in varicella/influenza risk of Reye syndrome
 - APAP (Acetaminophen): no association with Reye syndrome. Not intrinsically anti-inflammatory. Most commonly used drug for pediatric analgesia
 - Opioids: for moderate to severe pain not responsive to above medications. Cardio-respiratory depressive effects may be greater in children especially infants <3 mos, ex-prematures <60 wks post-gestational age, children with airway anomalies, cardiac disease, neurologic disease, renal disease
 - Adjunctive analgesics: consider anxiolytics, antidepressants (SSRI, TCA), anticonvulsants (gabapentin), NMDA receptor antagonist, neuroleptics, a₂ agonist (clonidine, dexmedetomidine)
 - Regional anesthesia (epidural analgesia and peripheral nerve blockade):

- Involve pain/anesthesia service
- Onset, duration, potency, effect, systemic absorption, risk of side effects vary with drug selected and site of infiltration
- Complications best avoided by appropriate selection of drug and dose, appropriate technique
 - Utilize nerve stimulator, ultrasound, pressure gauge, landmarks, experience to minimize intraneural injection, intravascular injection among other complications
 - Epidural complications include epidural hematoma/abscess (surgical emergency), hypotension, unintentional intrathecal injection (spinal)
- Esters (chloroprocaine, benzocaine). Shorter duration, greater risk of allergy
- Amides (lidocaine, bupivacaine, ropivacaine, mepivacaine). Longer duration, greater risk of neurologic and cardiac side effects
- Lidocaine: commonly used for local and regional techniques. Rapid onset, moderate duration
- Bupivacaine: slow onset, long duration. Greatest risk of ventricular arrhythmias
- Additives:
 - Epinephrine: decreases uptake of local anesthetic. Avoid in end-arterial beds (penis, digits, pinnae, nose)
 - Bicarbonate: increases onset for most anesthetics
- EMLA cream: apply to intact skin 30–45 min prior to procedure. Avoid in infants (risk of methemoglobinemia)
- Patient-controlled analgesia (PCA): requires patient/parental understanding, willingness, physical ability, and appropriate nursing/physician supervision; nurse-controlled analgesia (NCA) is an alternative.
- Non-pharmacologic modalities: acupuncture, music therapy, physical therapy, massage, TENS, biofeedback, relaxation techniques

Pediatric sedation

- Sedation is a continuum. Deeper sedation = inc. loss of protective airway reflexes, cardiorespiratory depression
- Moderate "conscious sedation": light sedation, patient maintains airway reflexes and drive to breathe, able to follow verbal commands. Often not sufficient for painful procedures
- Usually performed with reversible sedatives (benzodiazepines and opioids)
- History and physical examination, airway evaluation
- Obtain informed patient/parental consent; follow institutional guidelines
- Monitoring requirements: O₂ Sat, EKG, BP, adequacy of respiration, ETCO₂
- Always available: resuscitation drugs (code drugs, reversal agents, intubation drugs), O₂ and positive pressure delivery system (e.g., ambubag), suction, intubation equipment (SOAP = suction, oxygen, airway, pharmacy)
- Medications typically delivered IV, IM, PO, PR. Acquire IV access if feasible
- Practitioner must be familiar with and certified to administer drugs, monitoring depth of sedation/anesthesia, trained in resuscitation and airway management
- Fasting guidelines:
 - Solids/particulates/fatty meals/milk: 8 hrs
 - Formula/juice (with pulp): 6 hrs
 - Breast milk: 4 hrs
 - Clear liquids (apple juice, water): 2 hrs

- Drug classes:
 - Benzodiazepines (BZD): produce sedation and amnesia. No inherent analgesic properties. Cardiorespiratory depression possible especially in combination with opioids. Reversible with flumazenil
 - Barbiturates: cardiorespiratory depressant. No inherent analgesic properties. Possible histamine release (thiopental)
 - Opioids: often used in combination with other drugs for sedation especially BZD. Respiratory depression, bradycardia, chest wall rigidity (fentanyl). Reversible with naloxone. Morphine can cause histamine release
 - Other IV sedative/hypnotics
 - Propofol: excellent sedative. Antiemetic properties. Vasodilator/hypotension.
 Apnea/respiratory depression common. Avoid in soy/egg yolk allergy. Propofol infusion syndrome
 - Ketamine: dissociative (separates consciousness from physical perception). Dysphoria possible (may be less common with children). Often used with BZD. Good analgesic. Little respiratory depression in slow titrated dosing. Bolusing can cause apnea. Bronchodilator. Can raise blood pressure, ICP, and IOP. May decrease seizure threshold. Small risk of laryngospasm; can increase secretions
 - Etomidate: short acting. Respiratory depression. Adrenal suppression. No inherent analgesic properties. Temporary dystonic movements
 - Dexmedetomidine: intermediate acting. No respiratory depression; has sedative, analgesic and amnestic properties

Procedures (also see Chapters 39 and 40)

Extracorporeal membrane oxygenation

- External membrane system utilized to correct hypercapnia and hypoxemia; provides hemodynamic support
- Allows lower FiO₂ and ventilator pressures thus decreasing pulmonary injury
- Criteria for use in hypoxemic respiratory failure
 - Potentially reversible
 - Lack of response to conventional measures
 - Severe hypoxemia
 - $P_aO_2 < 50$ mm Hg despite high FiO_2 and high PEEP
 - $P_aO_2/FiO_2 < 100$
 - IO > 40 [OI = $(FiO_2 \times MAP/P_aO_2)$]
 - $Q_s/Q_t > 0.5$
 - Elevated mean airway pressures (MAP)
 - Cardiovascular depression with shock (pH < 7.25)
- Venoarterial: venous access via right internal jugular vein draining right atrium; arterial return via right common carotid artery to aortic arch or via femoral artery. Flow rates usually 80–150 ml/kg/min
 - Increased afterload on left ventricle
 - Arterial particulate and air emboli possible
 - Ligation of carotid artery often occurs with decannulation

- Venovenous: cannulation of jugular or femoral veins
 - Maintains normal pulsatile arterial flow
 - SpO₂ usually less than VA-ECMO
- Flow begun gradually to minimize fluid shifts, hyperkalemia, and disequilibrium syndrome
- Anticoagulation with heparin to reduce clotting of circuits and potential thrombotic emboli, may require AT3 (especially infants)
- Platelet consumption by circuit. Might require platelet transfusion
- Complications: coagulopathy, intracranial hemorrhage, neurologic deficits, seizure

Drug and Blood Product Dosing (Pediatrics)

• Note: Drug dosing should be tailored to individual clinical scenarios. Dosages outside these guidelines might be clinically appropriate

Analgesics	IV Dose (max)
Fentanyl	0.5–2 mcg/kg IV or 0.5–2 mcg/kg/hr IV gtt
Morphine	0.05–0.1 mg/kg IV or 0.05–0.1 mg/kg/hr IV gtt
Hydromorphone	0.015 mg/kg IV
Ketorolac	0.25-0.5 mg/kg (30 mg) IV
Flumazenil	0.01 mg/kg (0.2 mg) IV
Naloxone	0.1 mg/kg IV
Ibuprofen	10 mg/kg q6h PO (40 mg/kg/d)
Acetaminophen	10–15 mg/kg q4h PO (75 mg/kg/d)

PCA	Bolus (mcg/kg/dose)	Lockout (min)	Max Dose (mcg/kg)
Morphine	10–30	7–10	0.1-0.15
Fentanyl	0.5-1.0	7–10	0.015-0.02
Hydromorphone	3–5	7–10	0.002-0.004

Anticonvulsants	IV Dose
Diazepam	0.1–0.2 mg/kg IV 0.5 mg/kg PR
Lorazepam	0.1 mg/kg (max 4 mg) IV; repeat 5 min
Fosphenytoin	20 mg PE/kg (max 1,000 mg) IV, PE = phenytoin equivalents, give over 7 min
Phenobarbital	20 mg/kg (max 1,000 mg) (load) over 20 min IV, repeat 5 mg/kg dose prn to max 40 mg/kg; then 2.5 mg/kg IV/PO q12h
Levetiracetam	30 mg/kg IV over 15 min, then 10-20 mg/kg/dose IV/PO q12h
Pentobarbital	Therapeutic coma: 1–5 mg/kg IV over 1–2hr (load); then 1 mg/kg/hr IV may increase to 5 mg/kg/hr to achieve burst suppression on EEG, monitor hemodynamics

Blood Products	
Albumin 5%	10 ml/kg (0.5 g/kg)
pRBC	10 ml/kg
FFP	10–15 ml/kg
Platelets	1 unit/10 kg to raise 50,000
Cryo	1 unit/10 kg

Bronchodilators	
Albuterol	Intermittent: (0.5%) <10 kg 0.25 ml INH; 10–30 kg 0.5 ml; >30 kg 1 ml q1–6h Continuous: 0.5 mg/kg/hr (max 20 mg/hr) INH
Ipratropium	0.25-0.5 mg INH × 3; then q4-6
Racemic epinephrine (2.25%)	0.25-0.5 ml INH q1h
Terbutaline	Bolus: 10 mcg/kg IV over 10 min; then 0.4-10 mcg/kg/min
Magnesium sulfate	25-50 mg/kg (max 2 gm) IV over 20 min

Cardiac Drips		
Dobutamine	2.5-20 mcg/kg/min IV	
Dopamine	2.5–20 mcg/kg/min IV	
Epinephrine	0.05-2 mcg/kg/min IV	
Milrinone	50 mcg/kg IV load; then 0.25-0.75 mcg/kg/min	
Norepinephrine	0.05-1 mcg/kg/min IV	
Phenylephrine	0.1-0.5 mcg/kg/min IV	

Code Drugs	Dose
Adenosine	0.1 mg/kg (initial max 6 mg) rapid IV; if no effect, 0.2 mg/kg (max 12 mg)
Amiodarone	5 mg/kg (max 300) IV/IO bolus; may repeat \times 2
Atropine	0.02 mg/kg (min 0.1 mg/max 1 mg)
10% Calcium choride	20 mg/kg (max 2 gm) slow IV (central)
10% Calcium gluconate	100 mg/kg (max 2 gm) slow IV (central)
Dextrose	D50W: 1–2 cc/kg D10W: 5–10 cc/kg
Epinephrine	Cardiac arrest: IV/IO: 1:10,000 0.1 ml/kg (= 10 mcg/kg) (max 1 mg) q3–5min ETT: 1:1,000 0.1 ml/kg (100 mcg/kg) Anaphylaxis: IM (1:1,000) 0.01 ml/kg (= 10 mcg/kg) (max 500 mcg) Epi-pen 0.3 mg IM Epi-pen Jr. 0.15 mg IM
Lidocaine	1 mg/kg IV/IO/ETT (max 100 mg)
Magnesium sulfate	Torsades de pointes: 25-50 mg/kg IV/IO (max 2 gm)
Sodium bicarbonate	(8.4% = 1 mEq/ml)1 mEq/kg slow IV

Cardioversion/Defibrillation	
SVT or V tach with pulse	0.5-1 J/kg synchronized × 1; if no response, 2 J/kg
	2 J/kg × 1; if no response 4 J/kg

Intubation Dru	ıgs	
Propofol	1–3 mg/kg IV	
Thiopental	4–6 mg/kg IV	
Ketamine	0.5-2 mg/kg IV ; 3-7 mg/kg IM	
Fentanyl	1–5 mcg/kg IV	

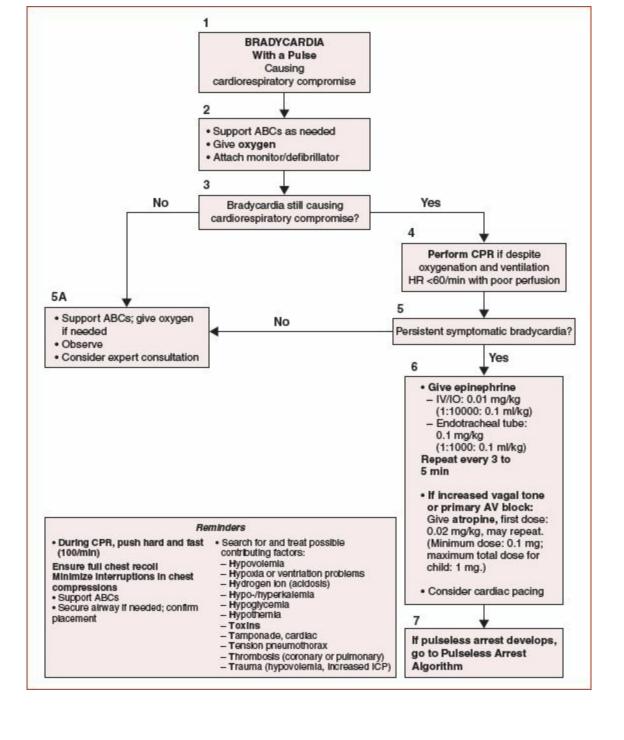
Neuromuscular Bl	ockers	
Vecuronium Rocuronium Succinylcholine	0.1-0.2 mg/kg IV 0.6-1.2 mg/kg IV 1-2 mg/kg IV 3-4 mg/kg IM Consider atropine premed if <5 yrs	

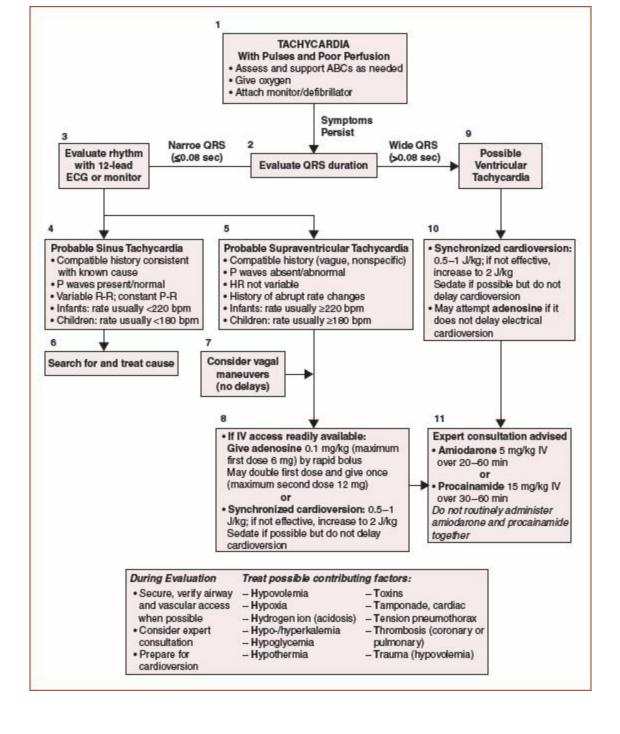
Sedative	Dose
Midazolam	0.05-0.1 mg/kg IV or 0.05-0.1 mg/kg/hr IV gtt
Lorazepam	0.05-1 mg/kg IV /PO q4h
Propofol	25–100 mcg/kg/min IV gtt (duration <12 hr, monitor for propofol infusion syndrome)
Dexmedetomidine	0.5–2 mcg/kg/hr IV gtt, consider 1 mcg/kg bolus over 10 min (monitor for bradycardia, hypo- or hypertension)

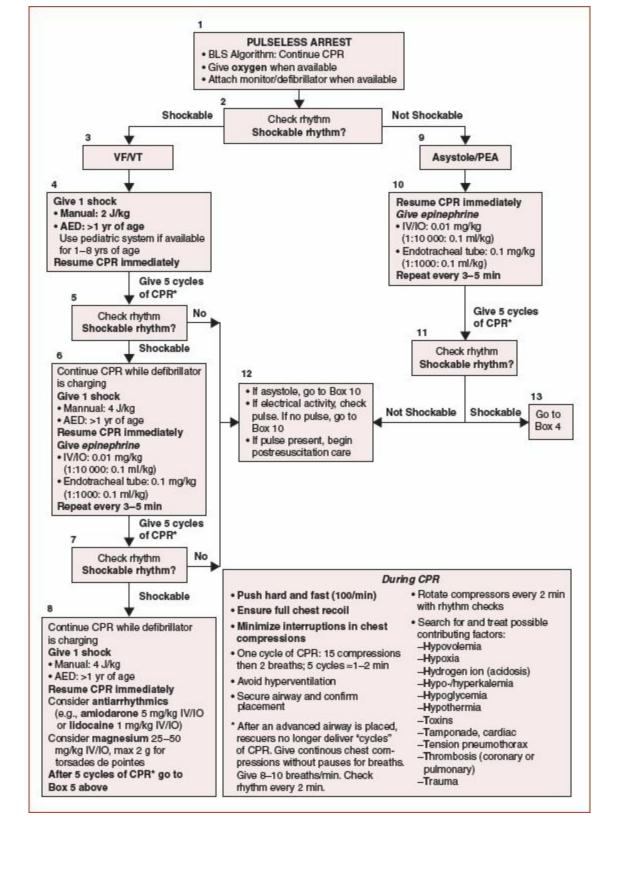
Steroids	Dose
Dexamethasone	0.1–0.6 mg/kg/dose (max 10 mg) IV/PO q8h Croup: 0.6 mg/kg IV/IM/PO × 1
Methylprednisolone	Load 2 mg/kg IV; then 1 mg/kg/dose IV q6-12h (max 120 mg)
Hydrocortisone	Stress dose 50 mg/m²/dose IV (max 100 mg); then 20 mg/m² IV q8h

• PALS (American Heart Association algorithms reused with permission from (*Circulation*. 2010;122:S729–S767))

- Sudden cardiac arrest in children is uncommon
- Cardiac arrest usually terminal event of progressive respiratory failure or shock
- Very high mortality
- Ventilation and oxygenation are initial priority







OBSTETRIC CRITICAL CARE

DIRK J. VARELMANN, MD

Rate of ICU admission pregnant/post-partum pt: 0.17%–1.1%. Most due to obstetrical complications (47%–93%): hypertension, hemorrhage, sepsis, respiratory failure

Aortocaval Compression Syndrome

- Compression of the inferior vena cava (IVC) and the aorta by the gravid uterus depending on position can occur after 16 wks of gestation
- In supine position the IVC is nearly completely compressed resulting in decreased right atrial filling pressure (decreased right ventricular preload)
- Symptoms: from mild hypotension to cardiovascular collapse
- Full lateral positioning relieves the symptoms in the majority of cases

Tocolytic-induced Pulmonary Edema

- Complication of sympathomimetic therapy (β_2 -mimetics, e.g., terbutaline; production of ritodrine discontinued in US) for premature labor
- Symptoms:
 - Dyspnea, tachypnea, hypoxemia
 - Cough, bibasilar crackles on auscultation (without heart failure)
 - Tachycardia, chest pain
 - Reduced hemoglobin concentration (hypervolemia from fluid resuscitation)
- Chest X-ray: bilateral diffuse interstitial opacities (pulmonary edema)
- Echocardiography: heart usually within normal limits for pregnant patient
- Treatment:
 - Discontinue β_2 -mimetics, consider other tocolytics
 - Supplemental O2, non-invasive ventilation in selected cases, intubation rarely required
 - Loop diuretics IV
 - Invasive hemodynamic monitoring rarely warranted
 - If pulmonary edema not improved within 12–24 hrs, exclude other causes
 - Mortality: very low

Aspiration

- Diagnosis
 - Frequently unnoticed, high level of suspicion required
- Treatment:
 - Milder cases resolve within 3–5 d with supportive therapy (antibiotic treatment and corticosteroids usually not indicated)
 - Aspiration pneumonitis can progress to full blown ARDS (see Chapter 5)

Venous Air Embolism

• Symptoms:

- Diaphoresis, restlessness
- Chest pain
- Dyspnea, tachypnea, hypoxemia
- Tachycardia, hypotension, cardiac arrest
- Auscultation: "mill wheel murmur"
- ECG: ST segment changes (depression more common than elevation)
- Treatment:
 - 100% O₂ (to hasten nitrogen removal from air bubbles)
 - Cardiocirculatory/ventilatory support
 - Patient can be placed in left lateral decubitus with Trendelenburg position (preventing air bubbles from blocking right ventricular outflow tract)
 - If central venous catheter is in place, aspiration of air can be attempted
 - Consider hyperbaric O₂ therapy in case of paradoxical cerebral air embolism

Fetal Monitoring

- Before a viable gestational age is reached, monitoring is limited to Doppler auscultation for fetal heart sounds
- Starting at 26 wks of gestational age, twice weekly assessment of fetal heart tones is recommended for high-risk conditions
- Testing should be performed for any changes in maternal status (e.g., inotrope/ vasopressor requirements, maternal acidosis, increase in oxygen requirements)
- Electronic fetal monitoring
 - For monitoring heart rate and uterine activity
 - Fetal heart rate variability occurs after 28 wks of gestational age
 - Maternal factor can lead to abnormal fetal heart rate without fetal distress
- Biophysical profile scoring measures:
 - Does not mature until 28-32 wks of gestational age
 - Recommended approach to assess fetal well being
 - Measures (with ultrasound):
 - Amount of amniotic fluid
 - Limb movement, tone, breathing efforts
 - Heart rate variability
 - Fetal growth

Pregnancy-related Diseases *Pre-eclampsia*

• Definition:

- Pregnancy-induced hypertension (PIH) with blood pressure >140/90 mm Hg, and
- Significant proteinuria with urine protein >300 mg/24 hrs
- Occurs after 20 wks of gestational age
- Usually resolves within 6 wks postpartum
- Cerebral complications if untreated (stroke, bleeding, edema)
- Hemodynamic changes:
 - Hypertension (high systemic vascular resistance, low cardiac output)
 - Low cardiac filling pressures

- Treatment
 - Manage blood pressure
 - Typically used antihypertensives:

Anti-hypert	ensives for the Treatment of Pregnancy-induced Hypertension (PIH)
Nifedipine	30-90 mg extended release PO qd
Hydralazine	10-40 mg IV q4-6h 10-50 mg PO q6h (max 300 mg/d)
Labetalol 20–80 mg IV q10 min, max 300 mg 200–400 mg PO bid (max 2,400 mg/d)	

- Maintain adequate volume status and urine output
 - Treat pulmonary edema if necessary
 - Renal failure is a rare complication, despite transient oliguria (resolves within 24–48 hrs postpartum)

Eclampsia

- Pre-eclampsia + convulsions
- Prodromal symptoms: headache, right upper quadrant pain
- Treatment:
 - As with pre-eclampsia
 - Magnesium sulfate for prevention and treatment of seizures
 - 4–6 g IV over 15–20 min (in 5 min if patient is seizing)
 - 1–2 g/h IV as maintenance dose
 - 2 g IV if seizures recur
 - Therapeutic level: 4-7 mEg/l = 2-4 mmol/l = 4.8-8.4 mg/dl
 - Magnesium therapy can be monitored by repeatedly checking patellar reflexes and respiratory rate (toxicity: loss of reflexes, respiratory arrest, cardiac arrest)
 - If seizures persist after second bolus of magnesium (2 g IV), use benzodiazepines or propofol. Intubation usually required
 - Expeditious delivery of the infant

HELLP

- HELLP syndrome: hemolysis, elevated liver enzymes, low platelet count
- Late findings: disseminated intravascular coagulation (DIC), pulmonary edema, placental abruption, retinal detachment, hepatic infarction/rupture
- Symptoms:
 - Right upper quadrant pain, nausea/vomiting, weight gain/edema
 - Symptoms of pre-eclampsia (elevated blood pressure, proteinuria)
- Laboratory abnormalities:
 - LDH > 600 IU/l (hemolysis), increased bilirubin, AST and ALT 200–700 IU/l, platelet count < 100,000 G/l, serum uric acid > 6 mg/dl
 - Blood smear shows schistocytes
 - Potential increase in BUN and creatinine (renal impairment)
- Treatment:
 - Delivery of the fetus

- Treatment of coexisting hypertension (labetalol, hydralazine)
- Magnesium (seizure prevention)
- Cesarean delivery is not mandatory (vaginal delivery may be appropriate)
- Complete blood count including platelets, LDH should be monitored for 48 hrs postpartum

Anaphylactoid Syndrome of Pregnancy

- Also known as amniotic fluid embolism (AFE)
- Rapid onset, during labor or delivery (or within 30 min afterwards)
- Foreign substance (e.g., amniotic fluid, fetal cell debris) enters maternal circulation, triggering the release of histamines and arachidonic acid derivates
- Symptoms:
 - Restlessness, confusion, hypoxia, hypotension, cardiac arrest, coagulopathy
- Treatment
 - Treatment is entirely supportive
 - Replacement of blood and clotting factors
 - Adequate volume replacement
 - Blood pressure support with vasoactive substances
 - Ventilatory support
 - Invasive monitoring (arterial and central venous catheters)

Peripartum Cardiomyopathy

- Heart failure in the last month of pregnancy or within 5 mos postpartum in the absence of identifiable cause/preexisting heart disease
- Symptoms/diagnosis
 - Ejection fraction <45%
 - Shortening fraction <30%
 - Left ventricular end-diastolic dimension >2.7 cm/m² body surface area
- Treatment
 - Reducing preload (diuretics), reducing afterload (vasodilators), improving contractility (inotropes)
 - Dietary sodium restriction
 - Cardiac transplant
 - Prognosis is poor if cardiac function does not improve within 6 mos postpartum

Sepsis/Septic Shock (see Chapter 10)

• Sepsis occurs in about 1 in 8,000 deliveries, mortality ~10%

Acute Fatty Liver of Pregnancy

- Symptoms:
 - Fulminant hepatic failure, coagulopathy, hepatic encephalopathy, coma
 - · Renal failure
 - Biopsy: deposition of microvesicular fat in hepatocytes (rarely performed, because of invasiveness of procedure and concomittant coagulopathy)
- Treatment:
 - Delivery of the fetus
 - Severe cases: liver transplantation

Ovarian Hyperstimulation Syndrome (OHSS)

- Associated with assisted reproductive technologies (ART), 0.2%–1% incidence
- Symptoms:
 - Nausea/vomiting, diarrhea, hemodynamic instability
 - Multiorgan failure (ARDS, acute renal failure, ascites)
 - Thromboembolism
- Treatment:
 - Daily monitoring of weights
 - Periodic laboratory measurements (electrolytes, complete blood count, human chorionic gonadotropic hormone HCG)
 - Fluid resuscitation (do not aggravate edema, ascites, pleural effusions)
 - Severe cases: repeated paracenteses, thoracenteses
 - Thromboprophylaxis (pneumatic compression stocking, heparin)
 - Most severe cases:
 - Mechanical ventilation, invasive cardiovascular monitoring
 - Short-term hemofiltration/hemodialysis
 - Early termination of pregnancy in critical cases

OBESITY: SPECIAL CONSIDERATIONS

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Classification	BMI (kg/m²)		
	Principal Cut-off Points	Additional Cut-off Points	
Underweight	<18.50	<18.50	
Severe thinness	<16.00	<16.00	
Moderate thinness	16.00-16.99	16.00-16.99	
Mild thinness	17.00-18.49	17.00-18.49	
Normal range	18.50-24.99	18.50-22.99	
	0.0000000000000000000000000000000000000	23.00-24.99	
Overweight	≥25.00	≥25.00	
Pre-obese	25.00-29.99	25.00-27.49	
		27.50-29.99	
Obese	≥30.00	≥30.00	
Obese class I	30.00-34.99	30.00-32.49	
		32.50-34.99	
Obese class II	35.00-39.99	35.00-37.49	
		37.50-39.99	
Obese class III	≥40.00	≥40.00	

Source: Adapted from WHO, 1995, WHO, 2000 and WHO, 2004.

Metabolic Syndrome

- Constellation of clinical phenotypes linked to cardiovascular diseases (see Table below). The core components are glucose intolerance or diabetes, obesity, hypertension, and dyslipidemia
- Other conditions associated with the syndrome include physical inactivity, aging, hormonal imbalance, and genetic predisposition
- Prevalence: 25%–34% of the US population depending on the definition used
- The metabolic syndrome does not necessarily predict an elevated cardiovascular disease's risk beyond the sum of its components nor does it provide better predictive power than the Framingham risk score (http://www.globalrph.com/atp_calc.htm)
- Current guidelines for the management of atherogenic dyslipidemia recommend lowering LDL-C to evidence-based target levels, with a subsequent focus on elevating HDL-C levels and reducing triglyceride levels
- In the absence of improved outcomes, perioperative beta blockade in metabolic syndrome can only be recommended for patients already receiving this therapy
- Perioperative administration of statins may reduce perioperative risk of cardiac events
- Diuretics and beta blockers in high doses can worsen insulin resistance and atherogenic dyslipidemia
- Adequate glycemic control is recommended with serum blood sugar target between 130 and 150 mg/dl. Tighter control runs the risk of hypoglycemia

Definitions of Metabolic Syndrome					
Organization	Waist Circumference or BMI	Triglyceride Level	HDL-C Level	Blood Pressure Value	Fasting Glucose Level
American Heart Association/National Heart, Lung, and Blood Institute	Men: ≥102 cm (40 in.) Women: ≥88 cm (35 in.)	≥150 mg/dl (1.7 mmol/l)	Men: <40 mg/dl (1.03 mmol/l) Women: <50 mg/dl (1.29 mmol/l)	≥130/85 mmHg or previous hypertension treatment	≥100 mg/dl
European Group for the Study of insulin Resistance	Men: ≥94 cm (37 in.) Women: ≥80 cm (31 in.)	≥178 mg/dl (2.0 mmol/l)	<40 mg/dl (1.03 mmol/l)	≥140/90 mm Hg	≥110 mg/dl (6.1 mmol/l)
International Diabetes Federation	Men: ≥94 cm Women: ≥80 cm	≥150 mg/dl (17 mmol/l)	Men: <40 mg/dl (1.03 mmol/l) Women: <50 mg/dl (1.29 mmol/l)	≥130/85 mm Hg or previous hypertension treatment	≥100 mg/dl (5.6 mmol/l)
National cholesterol Education Program Adult Treatment Panel III	Men: ≥102 cm (40 in.) Women: ≥88 cm (35 in.)	≥150 mg/dl (1.7 mmol/l)	Men: <40 mg/dl (1.03 mmol/l) Women: <50 mg/dl (1.29 mmol/l)	≥130/85 mm Hg	≥110 mg/dl (6.1 mmol/l)
World Health Organization	Waist to hip ratio Men: >0.90 Women: >0.85 or BMI > 30 kg/m ²	≥150 mg/dl (1.7 mmol/l)	Men: <35 mg/dl (0.90 mmol/l) Women: <39 mg/dl (1.00 mmol/l)	≥140/90 mm Hg	≥110 mg/dl (6.1 mmol/l)

Airway Management (also see Chapter 4)

- Potentially more difficult mask ventilation and intubation
- Optimal patient positioning and airway/equipment preparation is essential
- Risk factors for difficult intubation
 - Limited neck mobility and mouth opening
 - A short sternomental distance
 - A receding mandible and prominent teeth
 - Neck circumference >40 cm
 - Mallampati score of ≥3
 - Prior history of difficult intubation

Approach to Intubation (see Chapter 4)

Mechanical Ventilation

- Initial tidal volume calculated according to ideal body weight and then adjusted according to systemic arterial blood gases
- Addition of positive end expiratory pressure (PEEP 8–10 cm H₂O) facilitates alveolar recruitment and prevent atelectasis
- Limit transpulmonary pressure to ≤35 mm Hg
- Basilar atelectasis and VQ mismatch: most common causes of hypoxemia in intubated patients (may need to rule out PE, pneumonia, or pulmonary edema)
- S Maintain trials of spontaneous breathing during mechanical ventilation even in patients with severe pulmonary functional disorders
- Since morbidly obese patients are at higher risk for post-extubation stridor, may perform a cuff leak test for identifying laryngeal edema prior to extubation (has poor specificity)
- Extubate in semirecumbent position
- Use of bilevel non-invasive positive airway pressure at a level of 12/4 in the first 48 hrs post-extubation improves pulmonary function and oxygenation
- Application of CPAP should be initiated at the earliest opportunity post-extubation in those with prior diagnosis of obstructive sleep apnea

Fluid Loading Poorly Tolerated

• Each 1 kg/m² increase in BMI is associated with a 0.08 l/min increase in CO and 1.35 ml increase in SV. Poor tolerance of IV fluid load may be due to right heart strain secondary to existing pulmonary hypertension

Diagnostic Imaging

- Ascertain radius and weight limit of the operating/procedure table
- Chest radiograph shows limited diagnostic quality image with poor X-ray penetration and poor visualization of lung bases
- Use the lowest frequency transducer available (2 MHz) during sonography and position the transducer within the range of the focal length of the transducer
- MR scanners with a high signal-to-noise ratio (SNR) and strong gradients (≥1.5 T) cannot accommodate patients weighing >350 lb (159 kg). A vertical field open MRI system is needed for patients up to 550 lb (250 kg)

Venous Thromboembolism (VTE) Prophylaxis

- Enoxaparin, 40–60 mg subcutaneously BID
- Consider anti-Xa monitoring during LMWH treatment
 - With once daily dose, target a level of 1.0–2.0 IU/ml at 4 hrs post-injection
 - For twice daily administration, aim at a target of anti-Xa level of 0.6–1.0 IU/ml
- Alternatively, 7,500 units of unfractionated heparin $3 \times /d$ for BMI > 50; 5,000 units for BMI is < 50
- No randomized controlled trials demonstrate efficacy or mortality benefit of IVC filter placement over sequential compression devices, ambulation, or anticoagulation alone
- Indications for prophylactic filter placement include failure of anticoagulation therapy, known hypercoagulable state, decreased cardiopulmonary reserve, and BMI > 55

Nutrition

- Although obese patients have excess body fat, they are more likely to develop protein energy malnutrition
- Indirect calorimetry should be used to calculate energy expenditure
- If indirect calorimetry is not available, provide 20–30 kcal/kg of IBW/d
- Protein requirements should be aimed at achieving nitrogen equilibrium: 1.5–2.0 g/kg of IBW

Pressure Induced Rhabdomyolysis

- Rare but potentially serious complications after prolonged surgery
- Epidural anesthesia may mask symptoms of rhabdomyolysis of the lower limbs, gluteal or lumbar musculatures
- Compartment syndrome, acute renal failure, and myoglobinuria are potential sequelae
- When suspected, institute aggressive hydration and dieresis with mannitol to a target urine output of 1.5 ml/kg/hr
- Alkalinize urine with sodium bicarbonate to a pH > 7.0 (controversial)

Nursing Care

- Provide instructions for the staff on available equipment and techniques and the importance of securing help before to lifting the obese to avoid work-related injury
- Do not rely on rotational mattresses to relieve pressure
- Unconscious, immobile patients are prone to yeast infections in the skin folds
- It is advisable that morbidly obese patients be triaged to receive tests early in the day when the largest number of staff are available to move and secure the patient

Drug Therapy

Antibiotics	Recommended Weight for Dosing
β-lactam	IBW* + 0.3 (ABW - IBW)
Vancomycin	ABW
Fluoroquinolones	IBW + 0.45 (ABW - IBW)
Gentamicin	IBW + 0.43 (ABW - IBW)
Tobramycin	IBW + 0.58 (ABW - IBW)
Amikacin	IBW + 0.38 (ABW - IBW)
Erythromycin	IBW
Sulfonamide	IBW
Acyclovir	IBW
Amphotericin	ABW
Fentanyl	$52/(1 + [196.4 \times e^{-0.025 \text{ ABW}} - 53.66]/100)$
Propofol	ABW
Benzodiazepines Single dose Continuous infusion	ABW IBW

Adapted from Wurtz et al. Antimicrobial dosing in obese patient. Clin Infect Dis. 1997;25:112–118. IBW, ideal body weight; ABW, actual body weight.

^{*}IBW (kg) for men = 50 kg + $(2.3 \times \text{height in inches over 60 in.})$

^{*}IBW (kg) for women = $45.5 \text{ kg} + (2.3 \times \text{height in inches over } 60 \text{ in.})$

- Increased ratio of adipose to lean body mass alters volume of distribution (Vd)
- Accumulation of lipophilic drugs in adipose tissue increases the dose necessary to achieve effect, and prolongs the elimination half-life. Dosing of these drugs in obese patients is generally approximated best using actual body weight (ABW) rather than the ideal body weight (IBW)
- The Vd of hydrophilic drugs in general relates better to lean body mass (approximated by IBW) because of poor penetration into adipose tissue

THE ELDERLY: SPECIAL CONSIDERATIONS

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First level assessment for functional, cognitive impairment, and polypharmacy at admission

Functional Status Assessment

Baseline functional impairment is associated with in-hospital delirium, and increased 1-yr mortality. In addition, the inability to regain baseline function during hospitalization is an independent risk factor for 3-mo mortality in elderly patients.

Activities of Daily Living (ADLs): bathing, dressing, transferring, toileting, continence, feeding (asking the patient or the family) (Gerontologist. 1970;10:20–30)

Scoring:

- Complete without assistance (score 1)
- Complete with assistance (score 2)
- Unable without assistance (score 3)

Consider a patient as dependent if unable to complete daily tasks without assistance in >2 ADLs

Action:

Consider a patient who receives assistance in ADLs as at risk of functional decline during and after the hospitalization. Order early physical and occupational therapy. (Lancet 2009;373: 1874–1882)

Instrumental Activities of Daily Living (IADLs): [asking the patient or the family] (Gerontologist.1969;9:179–186; Geriatrics at your Fingertips, 12th ed., 2010)

- Use the telephone
 - Operates phone on own initiative (score 1)
 - Dials a few well-known numbers (score 1)
 - Answers telephone but does not dial (score 1)
 - Does not use the telephone (score 0)
- Shopping
 - Takes care of all shopping (score 1)
 - Shops independently for small purchases (score 1)
 - Needs to be accompanied on any shopping trip (score 1)
 - Completely unable to shop (score 0)
- Preparing meals
 - Plans, prepares and serves meals (score 1)
 - · Prepares meals if supplied with ingredients (score 1)
 - Heats and serves prepared meals (score 1)
 - Needs to have meals prepared and served (score 0)
- Housekeeping
 - Maintains house alone or with occasional assistance (score 1)
 - Performs light daily tasks (e.g., dishwashing) (score 1)
 - Performs lightly daily task but no acceptable level of cleanliness (score 1)
 - Needs help with all home maintenance (score 1)
 - Does not participate in any housekeeping tasks (score 0)
- Doing laundry
 - Does personal laundry completely (score 1)
 - Launders small items (score 1)
 - · All laundry must be done by others (score 0)
- Using public transportation or driving
 - Travels independently (public transportation or drives) (score 1)
 - · Arranges own travel via taxi (score 1)
 - Travels on public transportation when assisted (score 0)
 - Travels limited to taxi or automobile when assisted (score 0)
 - Does not travel at all
- Handling finances
 - Manages financial matters independently (score 1)
 - Manages day-to-day purchases but needs help with banking etc. (score 1)
 - Incapable of handling money (score 0)

- Handling medications
 - Is responsible for taking medications (score 1)
 - Takes responsibility if medications are prepared (score 0)
 - Is not capable of dispensing own medications (score 0)

Scoring:

Give 1 point for each type of activity. Add the total points from each type of activity. The total score ranges from 0 to 8.

Women

- 7–8 = high level of independence
- 5-6 = moderate level of independence
- 3–4 = moderate level of dependence
- 1-2 = dependence

Men

- 5 = independence
- 4 = moderate independence
- 3 = minimal independence/dependence
- 2 = moderate dependence
- 1 = dependence

Action:

Provide early occupation therapy for every patient but especially for those with moderate independence, minimal independence/dependence, and moderate dependence. (Lancet 2009;373: 1874–1882)

Cognitive Status Assessment

The presence of baseline cognitive impairment poses the patient at higher risk for delirium during the hospitalization, and increased mortality. Patients with dementia who experience delirium are more likely to have an accelerated decline in their cognitive performance and are more sensitive to polypharmacy.

Ask the family if there is a known baseline cognitive impairment. If patient is communicative and not delirious perform a short evaluation of their cognitive abilities with the Mini Cog. Mini Cog combines a 3-item recall test with a clock-drawing test (CDT) (Int J Geriatr Psychiatry. 2000;15:1021).

Step 1: instruct the patient to listen carefully to and remember 3 unrelated words (e.g., apple, penny, table) and then to repeat the words.

Step 2: instruct the patient to draw the face of a clock on a blank sheet of paper. After the patient puts the numbers on the clock face, ask him or her to draw the hands of the clock to read a specific time, such as 11:20. These instructions can be repeated, but no additional instructions should be given. Give the patient as much time as needed to complete the task.

Step 3: ask the patient to repeat the 3 previously presented words.

Scoring:

Give 1 point for each recalled word after the CDT distractor

- A score of 0 indicates positive screen for dementia
- A score of 1 or 2 with an abnormal CDT indicates positive screen for dementia
- A score of 1 or 2 with a normal CDT indicates negative screen for dementia
- A score of 3 indicates negative screen for dementia

Action

If the screening is positive without the presence of delirium, consider this patient at high risk for delirium and behavioral-psychological symptoms of dementia (BPSD)

Medications (Polypharmacy) Assessment

Medications

Adverse drug events are frequent in elderly patients. Review pre-admission medications, see Polypharmacy below.

Frailty

Frailty is a clinically recognizable state of aged people who are at increased risk of adverse outcomes such as onset of disability, morbidity, institutionalization, or mortality as a consequence of a diminished ability to respond to stress. (J Nutr Health Aging. 2008;12:29–37)

Define the presence and degree of frailty:

Obtain ADL and IADL information along with medical history and then score the patient according to the Rockwood Frailty Scale (CMAJ. 2005;173:489)

Scoring:

Score	Category	Description
1	Very fit	Robust, active, energetic, well motivated and fit; these people commonly exercise regularly and are in the most fit group for their age
2	Well	Without active disease, but less fit than people in Category 1 (above)
3	Well, with treated comorbid disease	Disease symptoms are well controlled compared with those in Category 4 (below)
4	Apparently vulnerable	Although not frankly dependent, these people commonly complain of being "slowed up" or have disease symptoms
5	Mildly frail	With limited dependence on others for instru- mental activities of daily living such as grocery shopping, cooking, and housekeeping
6	Moderately frail	Help is needed with both instrumental and non- instrumental activities of daily living
7	Severely frail	Completely dependent on others for activities of daily living, or terminally ill

Actions:

- If a patient is classified as frail then a referral should be made for a geriatrics-focused interdisciplinary management: geriatric evaluation and management (GEM), comprehensive geriatric assessment (CGA) (Lancet. 1993;342:1032–1036)
- The post-ICU in-patient management should be delivered in an Acute Care for Elderly Unit (ACE unit). (NEJM. 1995;332:1388; J Am Geriatr Soc. 2000;48:1572)

Risk of Falling

Assessing the Risk of Falling

First level screening. Ask the patients or family: (AGS Practice Guidelines. 2010)

- 1. If there have been 2 or more falls in the last 12 months
- 2. If there have been difficulties with balance or walking

Scoring:

If the answer is positive to any of these questions then consider the patients at risk of falling.

Action:

If a patient is at risk of falling refer to the specific section on falls (geriatric syndrome) in this chapter for further advice.

Nutrition

Assessing the Nutritional Status

Ask the patient or family if the patient has lost any weight in the year prior to the current admission (JAm Geriatr Soc. 1995;43:329)

Scoring:

Malnutrition if at least 5% loss of usual body weight

Action:

Refer to the section on malnutrition and Chapter 12

Vision and Hearing

	Assessing Vision and Hearing
Vision	Difficulty driving, watching television, reading, or doing any of your daily activities because of eyesight, even while wearing glasses? (Am J Med. 1996;100:438)
	Scoring: If yes the screening is positive.
	Action: Provide the patients with their glasses.
Hearing	Ask the patient or the family the following questions screen (JAGS. 1998;46:1008): Is the patient older than 70 yrs? (1 point) Is the patient male? (1 point) Does the patient have 12 or fewer years of education? (1 point) Did the patient ever see a doctor about trouble hearing? (2 points)
	Without a hearing aid, can the patient usually hear and understand what a person says without seeing his face if that person whispers to you from across the room? (If no, 1 point)
	Without a hearing aid, can the patient usually hear and understand what a person says without seeing his face if that person talks in a normal voice to you from across the room? (If no, 2 points)
	Scoring: A score ≥3 represent a positive screening for hearing impairment.
	Action: Provide the patients with hearing aids if screening positive.

Depression

Assessing Preexisting Depression

Ask the family or the patient if over the past 2 wks, how often the patient has been bothered by little interest or pleasure in doing things? Feeling down, depressed, or hopeless? (Med Care. 2003;41:1284)

Scoring:

- A score of 0 if not at all
- A score of 1 if several days
- A score of 2 if more than half the days
- A score of 3 if nearly every day

Total score ≥3, positive screen for depression

Action:

Consider further evaluation or treatment

Daily Assessment: FAST HUGGS (CCM. 2005;33:1225-29; NEJM. 1995;332:1338-44)

- Feeding: can the patient be fed orally, if not enterally? If not, should we start parenteral
 feeding?
- Analgesia: the patient should not suffer pain, but excessive analgesia should be avoided
- Sedation: The patient should not experience discomfort, but excessive sedation should be avoided; "calm, comfortable, collaborative" is typically the best level. Try to avoid benzodiazepines use.
- Thromboembolic prevention: Should we give low-molecular-weight heparin or use mechanical adjuncts?
- Head of the bed elevated: Optimally, 30° to 45°, unless contraindications (e.g., threatened cerebral perfusion pressure)
- Ulcer prophylaxis: usually H₂ antagonists; sometimes proton pump inhibitors (consider the risk of increased of clostridium difficile infection) (Arch Int Med. 2010;170:772-8)
- Glucose control: maintain a blood glucose target of 180 mg/dl or less and avoid hypoglycemic episodes (NEJM. 2009;360:1283–97)
- Geriatric: delirium evaluation, ADL evaluation, early mobilization, early occupational and physical therapist, review of medications, removal of restraints (e.g., lines, physical restraints, chemical restraints, urinary catheters)
- Social: involvement of social worker, DNR/DNI orders

GERIATRIC SYNDROMES IN THE ICU

Delirium

Delirium management in the ICU see Chapter 8.

Dementia: Differential Diagnosis

Use the following features to differentiate between delirium, dementia and depression. (*ICM*. 2008;34:1907)

Feature	Dementia	Delirium	Depression
Onset	Slow	Sudden	Variable
Duration	Years	Day or weeks	Variable
Reversibility	Persistently progressive	Fluctuating	Variable during the da
Variation at night	Worse	Almost worse at night	Generally none
Level of consciousness and orientation	Impaired and worsen- ing in the last stages	Fluctuates, disoriented	Generally normal
Attention and memory	Attention usually retained in the early phase, and early loss of short-term memory	Inattention and poor short-term memory	Intact memory, may have poor attention
Cognition	Global cognitive impairment	Focal to global cognitive deficits	Impaired in severe stage and may be misdiagnosed as dementia
Psychotic symptoms	Less frequent	Hallucinations might be present (mostly visual), delusions and illusions	Rare: psychotic ideation is complex and related to the mood of the patient
Speech	Difficulty finding words	Often incoherent words	Normal
EEG	Variable	Generalized diffused slowing	None

• If cognitive impairment is newly detected at ICU admission or at ICU discharge, consider referring the patient to a memory clinic or to geriatric clinic for further assessment

Behavioral and Psychological Symptoms (BPSD) of Dementia

- Agitation/aggression, psychosis (hallucinations or delusions) and mood disorders (depression) are the most common BPSD. In patients with Lewy bodies dementia and Parkinson's dementia visual hallucinations, delusions and depression are more frequent
- Step 1: (Am J Alzheimers Dis Other Demen. 1996;11:10)
 - Evaluate the presence of pain, new infection (e.g., respiratory or urinary tract infections), constipation, dehydration, hunger, thirst, sleep disruption, and environmental factors (noise, light); consider visual/auditory impairments
 - Perform a thorough evaluation of pharmacologic treatments. Review medication records because discontinuation of cholinesterase inhibitors (e.g., donepezil) might be associated with worsening BPSD (*Neurology*. 2004;63:214)
- Step 2: non-pharmacologic management of BPSD (Am J Psychiatry. 2005;162:1996)
 - Provide calming music and aromatherapy
 - Provide sensory stimulation (physical touch, gentle massage) through family members and create a home-like atmosphere
 - Decrease light and noise level
 - Approach the patient frontally and use a relaxed demeanor and a smile (*J Gerontol*. 1992;47:242)
 - If the presence of BPSD poses significant danger and non-pharmacologic approaches have not been beneficial then consider a pharmacologic treatment
- Step 3: pharmacologic management of BPSD

- "Start slow and go slow" (Psychiatry Clin North Am. 1997;20:205)
- In case of Agitation/Aggressive Behavior/Psychosis consider options:
 - Olanzapine: start with 2.5 mg/d and titrate up to 5 mg/d
 - Risperidone: start with 0.5 mg/d and titrate up to 1 mg/d
 - Citalopram: 20 mg/d
 - Careful use of antipsychotics in Lewy bodies dementia for higher risk of neuroleptic malignant syndrome (*JAMA*. 2005;293:596)
 - Lower dose/discontinue antipsychotics when acute symptoms are controlled
- In case of symptoms of depression:
 - Sertraline might be considered at 25 mg/d and titrate up to 150 mg/d (*Arch Gen Psychiatry*. 2003;60:737)

Malnutrition (see Chapter 9)

Falls

- The **Morse Fall Scale Score** could be used to further stratify the risk of falls during the ICU course (*Can J Public Health*. 1986;77:21)
- If a patient is at risk of fall then activate the fall prevention system in place in your ICU
- An elderly patient who is at risk of falling should be referred to a geriatrician for a **multifactorial fall risk assessment** to evaluate the history of falls, medications, gait-balance and mobility, visual acuity, other neurologic impairments, muscle strength, heart rate and rhythm, postural hypotension, feet and footwear, environmental hazard. (*AGS Practice Guidelines*. 2010)

Polypharmacy

- Assess for polypharmacy and inappropriate medications at multiple times, including ICU admission, during the ICU stay and at ICU discharge. Discontinue those that can be safely eliminated.
- Evaluate for the presence of potentially (PIMs) and actually inappropriate medications (AIMs) in particular anticholinergies drugs, antipsychotics, opioids. (*Arch Intern Med.* 2011;171:1032–4). PIMs are judged as AIMs according to their indication, effectiveness, dosages, and drug interactions. (*J Clin Epidemiol.* 1992;45:1045)
- Pay attention to the number of medications since a patient taking 2 drugs face 13% risk of adverse drug–drug interactions, 38% for 4 drugs, 82% if 7 or more drugs are simultaneously administered. (*Am J Emerg Med.* 1996;14:447)
- Assess the anticholinergic burden for its potential effects on cognitive function
- Assess the risk for adverse drug events with the following risk score

Assessing the Risk of Adverse–Drug Reactions (ADR)

Variable	Points
≥4 comorbid conditions	1
Heart failure	1
Liver disease	1
Number of drugs	
≤5	0
5–7	1
≥8	4
Previous ADR	2
Renal failure ^a	1
Scoring: The risk of ADR increases from 2.09	% with a score of 0–1 to 21.7% with a score ≥8

^{*}Defined a glomerular filtration rate <60 ml/min.

First Level Assessment at ICU Admission (5 min):

- Functional status (ADL, IADL)
- Cognitive status (family interview, Mini Cog)
- Medications review (anticholinergics drugs, ADR



Second Level Assessment (within 24 hrs of ICU admission):

- Frailty scale
- · Risk of falling
- Nutrition
- · Vision and hearing impairments
- Depression



Geriatric Syndromes Management in the ICU:

Delirium

Dementia and differential diagnosis
Behavioral and psychological symptoms of dementia

Malnutrition

Falls

Polypharmacy and adverse drug events

ADL, activities of daily living, IADL, instrumental activities of daily living, ADR, adverse drug reactions.

TOXICOLOGY

HEIKKI NIKKANEN, MD

DECONTAMINATION

- Activated charcoal (AC)
 - Most widely used of any technique for gastrointestinal decontamination
 - Significant proven benefit in clinical trials has been difficult to demonstrate
 - Use of AC does carry the risk of aspiration pneumonitis
 - Limitations of AC poor adsorption of alcohols, acids, bases, metals
 - Adsorptive capacity of AC ~1 g of xenobiotic per 10 g of charcoal
 - Recommendation: single dose AC if the ingestion occurred within an hour
- Multiple dose activated charcoal (MDAC)
 - Some toxins have significant enterohepatic or enteroenteric recirculation
 - MDAC disrupts this cycle by adsorbing the substance as it passes though the intestinal mucosa
 - Consider for OD of sustained release preparations or medications known to form concretions
 - Risks are similar as those for a single dose of AC
- Watch for ileus

Toxins Amenable to MDAC	
Carbamazepine	
Dapsone	
Phenobarbital	
Quinine	
Theophylline	
Yellow Oleander	

- Whole bowel irrigation (WBI)
 - Method of propelling the intestinal contents rapidly through the gut
 - Indications:
 - Toxic ingestion of sustained-release preparations
 - Ingestion of a large amount of a highly toxic substance not well adsorbed by AC
 - Removal of drug packets from the intestine
- Enhanced elimination
 - HD and CVVH
 - Exchange transfusion
 - Plasmapheresis
 - Manipulation of urinary pH
 - Ion exchange resins
 - Indications
 - Low volume of distribution (Vd)

- MW < 500 daltons
- Some larger molecules with high flux dialyzers

Substances Amenable to Dialysis				
Conventional HD	High Flux HD			
Aspirin	Carbamazepine			
Toxic alcohols	Phenobarbital			
Lithium	Phenytoin			
Theophylline				
Valproic acid				

- Plasmapheresis or exchange transfusion
 - Indications
 - Toxin molecular weight too great for dialysis
 - Toxin highly protein bound
 - Patient cannot tolerate dialysis (infants)
 - Not in common use discuss with toxicologist
- Manipulation of urinary pH
 - Enhancing excretion of acidic substances in nephron
 - Limits diffusion back through the tubule by ionizing the molecule
 - Less able to pass through a lipid bilayer
 - Used in treatment of salicylate and uranium toxicity
 - Initial bolus sodium bicarbonate at 1–2 mEq/kg
 - Infusion of a solution of 132 mEq of sodium bicarbonate in 1L D5W at $1.5 2 \times \text{maintenance}$
 - Goal urine pH > 7.5
 - Arterial pH should not be allowed to exceed 7.55
 - Keep serum K above 4 mmol/l

METABOLIC TOXINS

Salicylates

- Compounds including:
 - Aspirin
 - Oil of wintergreen (methylsalicylate)
 - Pepto-Bismol (bismuth subsalicylate)
 - Others
- Kinetics
 - Readily absorbed in the small intestine
 - Low volume of distribution
 - Toxic-therapeutic window is relatively narrow
 - Half life increases significantly with small increases in dose
- Toxicity can be significant in either acute or chronic dosing
 - Mechanisms include uncoupling of oxidative phosphorylation
 - Results in metabolic acidosis, hyperthermia, and hypoglycemia

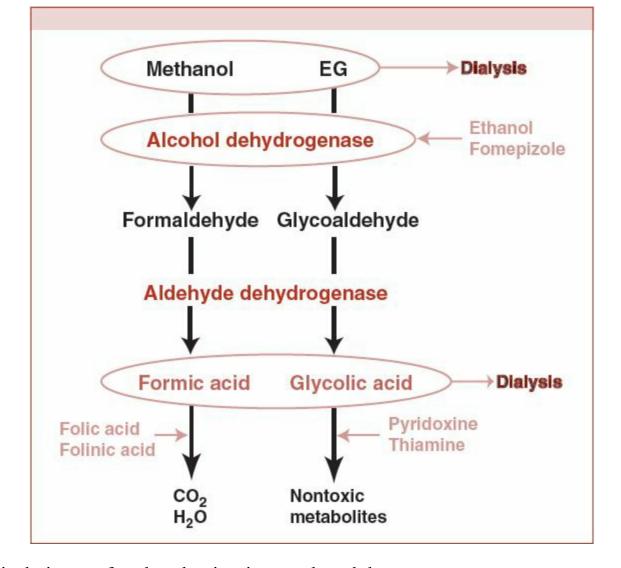
- Stimulation of the respiratory center results in hyperpnea and tachypnea
 - Primary respiratory alkalosis
- Increased capillary permeability causes pulmonary edema
- Clinical picture
 - Tachypnea and hyperpnea
 - Tinnitus (aspirin concentration above 30 mg/dl)
 - CNS effects from agitation to coma. Seizures possible
 - Hyperthermia
 - Nausea and vomiting
 - Pulmonary edema may be present
- Laboratory analysis
 - ABG shows primary metabolic acidosis and primary respiratory alkalosis
 - Anion gap is present
 - Aspirin concentration, ABG, basic metabolic panel should be repeated at 2 hr intervals
 - Done nomogram is not accurate at predicting morbidity or mortality. Absorption is erratic
 - Aspirin concentration >60 mg/dl in chronic or 90 mg/dl in acute toxicity are considered indication for dialysis. Concentration >30 mg/dl should prompt urine alkalinization
- Treatment
 - Supportive care
 - If patient is intubated, it is essential to maintain the minute volume as close to the patient's own efforts prior to intubation as possible. Failure to do so may result in acidemia and significant worsening of clinical picture. Sodium bicarbonate may be required to supplement ventilator efforts
 - Dehydration must be corrected, as many patients will be significantly volume depleted
 - Seizures can be treated with benzodiazepines or barbiturates
 - AC administration, even late after overdose, should be strongly considered. Patients with fluctuating aspirin concentrations may have an aspirin concretion present in the gut, and may benefit from multiple dose AC
 - Manipulation of urinary pH is useful to enhance elimination of aspirin
 - Correction of hypokalemia must be done concurrently
 - Consider hemodialysis for certain cases:
 - Concentrations as described above
 - Seizure or coma
 - Pulmonary edema
 - Renal failure
 - Refractory metabolic derangement

Toxic Alcohols

- Most common agents: methanol (MeOH) and ethylene glycol (EG)
 - Methanol is a solvent and component of windshield washing fluid.
 - EG is the base for a number of industrial chemical reactions and is present in automotive coolant.
 - Others include:
 - Isopropanol
 - Benzyl alcohol
 - Diethylene glycol

- Ethylene glycol ethers
- Toxic alcohols are metabolized by:
 - Alcohol dehydrogenase (ADH)
 - Aldehyde dehydrogenase (AlDH)
- Resulting in a metabolic acidosis and the formation of a toxin
- Rapidly and completely absorbed in the stomach and small intestine
- Not adsorbed by AC
- They both have volumes of distribution below 1 l/kg
- Figure 1 shows the metabolism of these alcohols to their toxic metabolites
- Majority of MeOH is converted to formate
- In cases where ADH has been inhibited, excretion of MeOH goes along 1st order kinetics, with a half life of 1–3 d
- EG is more readily excreted by the kidney
- Formate toxicity:
 - Damage to the retina from oxidant stress due to inhibition of cytochrome oxidase and depletion of glutathione
 - Ischemia or hemorrhage in the basal ganglia can also occur
- EG toxicity:
 - Oxalic acid precipitates with calcium to form crystals which primarily injure the kidney, although deposition of such crystals can be seen in a number of tissues
 - Tubular necrosis and cortical necrosis occur, although renal failure is usually reversible over weeks to months
 - Hypocalcemia, the other result of this reaction, can result in dysrhythmias and cardiovascular shock

Figure 1. The Metabolism of Toxic Alcohols to Their Toxic Metabolites



- Early clinical picture of methanol poisoning may be subtle
 - Its metabolism is slower than that of EG
 - Less inebriation than EG
 - GI symptoms are common
 - The hallmark of MeOH poisoning is 'snowy' or blurry vision
 - Headache, chest pain, and shortness of breath can occur
- Late clinical picture of MeOH poisoning
 - Coma or respiratory arrest ominous findings
 - Physical exam findings may include tachypnea, hyperpnea, dilated pupils, and hyperemia of the optic discs. Imaging of the brain may reveal infarction or hemorrhage of the basal ganglia
- Early clinical picture of EG poisoning
 - Inebriation
- Late clinical picture of EG poisoning
 - Coma or seizures
 - Cardiovascular toxicity, with QT prolongation, dysrhythmias and hypotension
 - AGMA develops
 - Oliguric renal failure occurs
- Laboratory analysis
 - Early after ingestion of a toxic alcohol may be normal unless the serum osmolality is measured and an osmolar gap is noted.
 - As the metabolism progresses, the osm gap gradually decreases and is replaced by an anion gap

- metabolic acidosis.
- An unexplained osmolar gap of 25 mOsm or more should prompt treatment for toxic alcohol poisoning and confirmatory testing
- Serum samples should be sent for gas chromatography/mass spectrometry analysis for toxic alcohols, but treatment should not be withheld while waiting for the results, which may take many hours
- Treatment
 - Correction of the metabolic acidosis with intravenous fluid and sodium bicarbonate.
 - All suspected or proven cases should receive antidotal therapy with fomepizole or ethanol to inhibit ADH
 - Hemodialysis removes the toxic alcohol, corrects acidosis, and removes the toxic metabolite. HD also removes ethanol and fomepizole, which means dosing must be adjusted accordingly
 - For MeOH, folinic acid at a dose of 1 mg/kg IV every 4 hr helps to metabolize formate
 - For EG, pyridoxine and thiamine should be given to help with metabolism of glyoxalic acid to nontoxic substances

Cyanide

- Sources
 - Cyanide is used in a number of laboratory and industrial processes
 - Product of combustion of a number of synthetic textiles, silk, and wool
 - Acetonitrile and acrylonitrile can cause delayed toxicity as they are converted to cyanide after absorption
 - Administration of sodium nitroprusside at high rates can result in elevated cyanide levels, especially in patients with hepatic or renal dysfunction
- Mechanism
 - Cyanide is considered a 'cellular toxin' as it inhibits mitochondrial cytochrome oxidase, disrupting aerobic metabolism
 - Tissues with high energy requirements or with great sensitivity to hypoxia are most affected
 - Lactic anion gap metabolic acidosis results
 - The clinical picture is one of shock and coma, although early on, restlessness or agitation may be seen
 - History is usually more important than the physical examination in making the diagnosis
 - Laboratory testing should include simultaneous ABG and VBG, as the inability of the tissues to extract oxygen results in similar pO₂ measurements in both samples. A lactate of above 8 mmol/l is a reasonable indicator of cyanide poisoning
- Management of toxicity
 - Supportive care and observation in patients with normal hemodynamic parameters and mental status.
 - More severely poisoned patients require antidotal therapy with hydroxocobalamin
 - Recently approved for use by the FDA.
 - Vitamin B12 precursor combines with CN- to form vitamin B12.
 - As effective as the previous three-part cyanide antidote kit, without the adverse effects of hypotension or the development of methemoglobinemia.
 - Secretions may be turned a reddish color, and certain laboratory measurements relying on colorimetric analysis may be affected

• Dose is 5 g IV infusion over 15 min, with a second equal dose to be given if clinical improvement is incomplete

NEUROTOXINS

Carbon Monoxide

- CO sources
 - Incomplete combustion of hydrocarbon fuel, whether that is charcoal, wood, gasoline or diesel, heating oil, natural gas, or propane
 - Methylene chloride, a solvent used as a dry cleaning agent and paint stripper. It is metabolized in the liver to form CO
- Mechanism of action of CO is complex
 - Binds to hemoglobin more avidly than oxygen
 - Impairs dissociation of oxygen from hemoglobin
 - Tissue effects which are more important from a pathologic standpoint
 - Binding to iron-containing proteins and enzymes such as myoglobin and cytochrome oxidase, which causes cellular hypoxia
 - Binding to endothelium and platelets releases nitric oxide, which causes vasodilation and the generation of peroxynitrate. This molecule has a number of pathologic effects on endothelial and lipid tissue
- Clinical picture of acute CO poisoning is confusing
 - Common nonspecific symptoms such as headache, weakness, or nausea
 - More severe cases may present with measurable end-organ dysfunction. Cardiac and neurologic findings, especially syncope and cerebellar abnormalities, are worrisome
 - Some neurologic abnormalities develop in the days to weeks after poisoning, and are termed delayed neurologic sequelae (DNS). Follow up neuropsychiatric testing should be arranged for severely poisoned patients
- Evaluation of the patient for CO toxicity
 - ABG or VBG with co-oximetry
 - Electrocardiogram
 - Chest radiograph
 - Lactate in case of smoke exposure
- Treatment with normobaric (NBO) or hyperbaric (HBO) oxygen
 - Equilibration of CO into the tissues from the blood takes hours, and enhancing the elimination can be done with oxygen
 - Measurement of COHb yields the concentration in the blood compartment, however, and the tissue effects are more significant. Therefore, a near-normal COHb in the setting of an exposure and an end-organ deficit should not exclude treatment
 - Use of HBO over NBO is somewhat controversial but most toxicology texts recommend its use
 - For ICU patients HBO should be strongly considered
 - Typically, a single treatment or dive is done, but can be repeated for persistent signs or symptoms. The only absolute contraindication to HBO is untreated pneumothorax

Lithium

- Kinetics: rapidly and completely absorbed in the small intestine
- Bimodal distribution, with an initial serum peak in the first few hours and subsequently a redistribution into the cells over the course of a week
- The Vd varies between 0.4 l/kg and 0.9 l/kg, and lithium is not bound to protein
- It is renally eliminated, with a half life from 12–48 hrs depending on serum concentration. Lithium overdose can be a result of an acute ingestion, an increase in dose, or worsening renal function
- Mechanism of action may block the effect of some neurotransmitters, and as it is a small cation, it may substitute for potassium or sodium in some cellular functions, with abnormal result
- Lithium toxicity in the acute setting is primarily neurologic, but attention should also be paid to cardiovascular examination

Intoxication	Mild	Moderate	Severe
Reflexes	Tremor	Hyperreflexia	Clonus
CNS	Confusion	Delirium, agitation	Seizures, coma
Non-neurologic	N/V/D	Tachycardia	Hyperthemia, hypotension

N/V/D: nausea, vomiting, diarrhea.

- Chronic lithium toxicity can cause significant renal dysfunction, including nephrogenic diabetes insipidus
- Laboratory testing
 - Serum electrolytes, electrocardiogram, and urine analysis
 - Lithium concentration should be drawn >6 hr after any acute ingestion to avoid an erroneously high result. There is poor correlation between lithium concentration and severity of poisoning in chronic or acute on chronic situations
- Treatment includes
 - Fluid resuscitation to maintain normal urine output
 - Benzodiazepines or barbiturates for agitation or seizure
 - Cooling for hyperthermia
 - Dialysis should be considered for patients with:
 - Severe symptoms
 - Renal failure
 - Lithium concentration >3.5 mEq/l in chronic toxicity
 - If dialysis is done, a repeat lithium level should be drawn 6 hr after dialysis, and the patient should be closely monitored for recurrence of symptoms

INH (Isoniazid)

- Kinetics
 - Rapidly absorbed from the small intestine
 - Volume of distribution of 0.6 l/kg
 - Metabolized by N-acetyltransferase (NAT)
- Toxicity
 - Inhibits pyridoxine phosphokinase, which converts pyridoxine to its active form
 - Binds to the active form, forming an inactive compound which is easily excreted
 - The resultant decrease in pyridoxine activity causes a decrease in gamma-aminobutyric acid (GABA) concentration and catecholamine synthesis
- Clinical picture

- Ingestion of as little as 2 g of INH in an adult can cause toxicity
- 10 g is considered a lethal dose without treatment
- GI symptoms predominate in the early stages
- Progression to cardiovascular collapse, metabolic acidosis, seizures, and coma
- Seizures are usually not controlled by anticonvulsant therapy
- Coma may persist for some time after the patient has been stabilized
- Laboratory analysis
 - Comprehensive metabolic panel
 - PT and PTT
 - Urine analysis
 - ABG or VBG
 - CK to evaluate for rhabdomyolysis
- Treatment
 - Ventilatory support, fluids, pressors
 - Sodium bicarbonate to correct metabolic acidosis
 - Benzodiazepines or barbiturates can be used for seizure
 - Pyridoxine antidote therapy
 - Dose equivalent to the ingested amount of INH should be given intravenously
 - If the amount is not known, 75 mg/kg of body weight can be used.
 - If the patient has refractory metabolic acidosis or renal failure, hemodialysis can be used to remove INH and treat the metabolic abnormalities

CARDIOVASCULAR TOXINS

Calcium channel blockers (CCBs)

- Kinetics
 - Absorption in the small bowel is rapid, Bioavailability is 90% or greater
 - There is first-pass metabolism, and blood concentrations reach a maximum within a few hours. Although there are five classes of CCB, three represent the majority of CCBs prescribed

Class	Agent			Activity
Phenykalkylamine	Verapamil			Cardiac and vascular
Benzothiazepine	Diltiazem			Cardiac
Dihydropyridine	Nifedipine	Nimodipine	Nicardipine	Vascular
Diarylpropylether	Bepridil			
Tertraline	Mibefradil			

- Mechanism of action
 - Variable activity on cardiac or vascular L type calcium channels is the basis for therapeutic activity of these medications, depending on which class of CCB is used
 - In overdose, receptor selectivity is lost, and even peripheral tissue calcium channels are affected in a clinically significant way
 - Supratherapeutic concentrations of calcium channel blockers also result in prolonged metabolism and excretion
- Clinical picture
 - Cardiac output decreases, SVR decreases, and bradycardia with AV block can be seen
 - Pulmonary edema may be due to reduced cardiac output, or direct effect on the pulmonary capillary endothelium
 - Blockade of L type calcium channels in the pancreas reduces the secretion of insulin, resulting in hyperglycemia. The degree of hyperglycemia can be used to predict the degree of toxicity
- Assessment of the patient
 - Baseline laboratory studies, with particular attention to the glucose and lactate
 - EKG which may show high degree AV blockade
 - Physical exam findings of peripheral vasodilation and warm skin consistent with distributed shock
- Treatment
 - Supportive care, which may require multiple pressors
 - Alpha-adrenergic agent for increasing vasomotor tone
 - Beta-adrenergic agent for increasing cardiac output
 - Amrinone may be useful, as it directly increases the opening of calcium channels via inhibition of phosphodiesterase III, resulting in an increase in cyclic AMP
- Bradycardia may be responsive to atropine. Cardiac pacing may yield in an increase in heart rate but has not been shown to increase blood pressure
- Calcium at high doses common strategies
 - Bolus dosing of calcium chloride at 1 g every 2–3 min until a response is seen
 - One gram every 15 min until the clinical response is seen, or until 4 doses have been given

- Continuous infusion at 0.2–0.4 mg/kg/hr, or titrated to a serum calcium of 8 mg/dl
- Glucagon provides increased cyclic AMP, via a G-protein-mediated mechanism
 - A bolus dose up to 10 mg until clinical improvement followed by an infusion of the effective total bolus dose, given every hour
- Hyperinsulinemia-euglycemia (HIE) therapy has been used as an effective antidote for CCB toxicity for a number of years
 - Its postulated mechanism includes increasing cellular uptake of glucose by making up for the decrease in insulin secretion as well as overcoming insulin resistance in the tissues
 - Bolus dosing of 0.5–1 U/kg is followed by continuous infusion of 0.5–1 U/kg/hr
 - Glucose should be checked frequently (q15 min) for the 1st hr, and at least hourly thereafter. Glucose may need to be given in bolus or continuous infusion
 - Potassium should be checked hourly and replenished as needed
- Intralipid, or lipid emulsion, is a component of parenteral nutrition which has been used as an antidote in the treatment of lipophilic toxins.
 - Most experience has been with systemic toxicity of local anesthetics
 - Has been tried as a last-ditch measure in severe poisonings of other types including CCB
 - One proposed dosing regimen is a bolus of 1.5 ml/kg of 20% lipid emulsion followed by an infusion at 0.25 ml/kg/min for 30–60 min
 - This therapy is clearly an off label use which should be reserved for extreme circumstances
 - Laboratory analysis of the blood may be made difficult by the lipid load for the next 12–24 hrs. Ultracentrifugation of the sample prior to analysis may be helpful
- Cardiac bypass or intra-aortic balloon pump can be used in very severe refractory cases

Digoxin

- Kinetics
 - Not very well absorbed in the GI tract in pill form
 - Vd of 5.6 l/kg. It is therefore not amenable to dialysis
 - It is renally excreted, with a half life of over 24 hrs. In overdose, this will be prolonged further
- Mechanism of action
 - In overdose, the sodium–potassium ATPase pump in cell membranes becomes dysfunctional, leading to an intracellular elevation in calcium and serum elevation in potassium
- Clinical picture
 - Conduction abnormalities including ectopy, tachydysrthymias, and bradydysrhythmias
 - Cardiogenic shock
 - Nausea and vomiting are common
 - Altered mental status or visual changes (yellowing of vision) can occur
- Laboratory analysis
 - Measurement of serum potassium is of use in determining the severity of poisoning
 - Mortality 35% with a potassium above 5 mEq/l and 100% in patients with potassium above 6.4 mEq/l
 - A digoxin concentration can be difficult to interpret, due to a number of factors
- Treatment
 - A combination of history of digoxin ingestion, a state of cardiac shock, cardiac dysrhythmia, and hyperkalemia (for acute ingestions) should prompt treatment for digoxin toxicity
 - Atropine or pacing for bradycardia

- Magnesium is of some theoretical benefit because it is thought to increase activity of the sodiumpotassium ATPase pump
- Antidotal treatment with digoxin-specific Fab fragments is the most important intervention. Calculation of the amount to administer depends on what is known about the ingestion

Antidotal Treatment	t with Digoxin-Specific Fab Antibody Fragments	
Known Data	Vials to be Given (Round up)	
Amount ingested	$(0.8 \times ingested amt in mg)/0.6 mg$	
Serum digoxin concentration	([digoxin] in ng/ml \times 5.6 l/kg \times pt weight kg/1,000)/0.6 mg	
Acute OD – empiric rx	10-20 vials	
Chronic OD – empiric rx	6 vials	

HEPATIC AND GI TOXINS

Acetaminophen

- Kinetics of acetaminophen (APAP) are predictable
 - Absorbed in the small bowel
 - Vd of 1 1/kg
 - The majority of APAP is conjugated and excreted renally. Only about 5% is metabolized via CYP2E1 and CYP1A2 to the toxic metabolite, n-acetyl-para-benzoquinone-imine (NAPQI). With therapeutic dosing and normal glutathione stores, NAPQI is rapidly metabolized and excreted
- Mechanism of action
 - In cases of overdose, glutathione is depleted and toxicity results
 - Exact mechanism is unclear but hepatic injury occurs in a centrilobular pattern
 - Mitochondrial dysfunction has been suggested as a mechanism

The clinical course of APAP poisoning has been artificially divided into four phases

Four Phases o	of the Clinical Course	Following Acetaminop	hen Toxicity
Phase I (Day 1)	Phase II	Phase III	Phase IV
Asymptomatic	LFTs rise further	Jaundice	Death or recovery
Nausea and vomiting	RUQ pain	Hepatic encephalopathy	(37.0
LFTs rise	Synthetic function off	MSOF	

- Diagnosis and treatment
 - On the basis of the history
 - Occasionally can be inferred from the physical examination and laboratory analysis
 - Use of Rumack–Matthews nomogram
 - If the ingestion occurred at a single point in time, and there were no co-ingestants which might interfere with gastric emptying, the nomogram can be used
 - If the APAP concentration as a function of time is above the possible hepatotoxicity line, treatment with n-acetylcysteine (NAC) should be initiated.
 - If the ingestion is complicated by co-ingestants or unclear timing, the nomogram cannot be used
 - APAP overdose patients admitted to the ICU typically have massive ingestion, liver synthetic dysfunction, or hepatic encephalopathy. They should be treated with NAC regardless of timing of

- ingestion or APAP level
- Dialysis can also be used to remove APAP in cases where the concentration is severely elevated (over 1,000 mcg/dl)
- Stopping NAC therapy in ICU patients should be done only when the LFTs are on a clear downward trend, with normal PT and PTT, and a zero acetaminophen level
- Dose and route of NAC should be chosen in conjunction with the hospital pharmacist or the local poison control center
- Chronic laboratory monitoring includes comprehensive metabolic panel, PT, and PTT, lactate, and VBG or ABG daily, or more often in cases of hepatic failure
- Criteria for liver transplantation are presented in the table below. Patients should be evaluated for transplant as soon as a concern develops

Criteria for Liver Transplantation	on Following Acetaminophen Toxicity
Arterial pH < 7.3	INR > 2 at 24 hr post ingestion
Serum creatinine >3.3	INR > 4 at 48 hr post ingestion
Initial lactate >3.5 mmol/l	INR > 6 at 72 hr post ingestion
Lactate after resuscitation >3.0 mmol/l	Grade III or IV encephalopathy

Caustics

Alkaline and acidic substances

- Drain cleaners, oven cleaners, automatic dishwasher detergents, brake dust removers, and other industrial chemicals
- Cause significant injury to the skin and mucosa
- Alkalis cause a so-called 'liquefaction' necrosis, as they cause softening of the tissues they come into contact with. This allows deeper penetration into the body
- Acids, on the other hand, cause a coagulation which can limit the depth of injury Ingestion of either substance can cause significant injury to the esophagus and stomach
- Burns to the GI tract are classified into 3 grades, and the progression of injury into 4 stages

	Three Grades of Burns in the Progression Follow	
Grade	Lesion	
1	Erythema	
2a	Superficial ulcers	
2b	Deep or circumferential ulcers	
3	Full thickness ulcers, necrosis	
Stage	Time	Pathophysiology
I	Minutes	Necrosis
II	Hours	Thrombosis
III	Days	Sloughing
IV	Weeks to months	Stricture formation

- Even brief skin contact with highly concentrated caustics can cause full thickness burns. In the days to weeks that follow an esophageal injury, tissue strength is diminished and perforation can occur
- Treatment

- No AC or gastric lavage, as they have not been shown to be of benefit. Lavage may damage tissues; AC can obscure the view during endoscopy.
- Steroid therapy is of no use in grade I injuries and can be harmful in grade III injuries. A prospective trial failed to demonstrate benefit in preventing strictures in patients including those with grade II injuries
- Early consultation of the gastroenterology and surgical services is essential in order to determine the extent of the injury. Perforation, which can be seen on chest radiograph or CT scan, usually requires prompt surgical intervention

DISASTER PREPAREDNESS

GEOFFREY S.F. LING, MD, PhD

BASIC PRINCIPLES

Casualty management begins with planning. The expected chaos surrounding any mass casualty situation necessitates being prepared with a well-rehearsed well-trained team.

If there is any suspicion of a CBRNE (chemical, biological, radiologic, nuclear, or explosive) event, ten casualty management begins with protecting medical providers (HazMat suits, etc.). A triage area seeds to have clean and unclean areas clearly identified with definitive demarcation lines. After roviding emergency care to save life and/or provide a rapid antidote, the patient must be econtaminated before proceeding to higher levels of medical care. A patient may then proceed into the redical treatment facility.

PLANNING

- Disaster plan needs to be in place at all times
- List of trained providers with 24/7 contact information
- Assembly point identified, must be specific location (cafeteria or staff lounge)
- Pre-determined tasks for key personnel
- Command structure with alternates for every key position, committees consisting of all involved disciplines, establish relationships with other medical treatment facilities
- Key medical groups: emergency medicine, trauma surgery, primary care, pathology, critical care, infectious disease, psychiatry, preventive medicine, pharmacy
- Other key groups: hospital administration, casualty/mortary affairs, engineering, patient administration, security, public affairs, clergy

TRIAGE

- This is a critical aspect of effective disaster management
- Formulate triage plan prior to any disaster or mass casualty
 - Triage Committee should include physicians, nurses, ethics, clergy, hospital administrator
 - Criteria for triage must be made well in advance of any disaster so as to ensure that all ethical issues are considered
 - Criteria must not be made by the triage officer at the time of disaster
- Triage area needs to be before and outside of treatment areas
- Triage Officer
 - Ideally ED/trauma physician but may be a critical care physician
 - If a contaminated environment, should be instead a non-physician (nurse, dentist, physician

- assistant, EMT)
- Empowered to make disposition decisions based on nature of injury, prognosis
- Must know patient load (anticipated and present), status of decontamination lanes, supply, evacuation chain, etc.
- Casualty sorting by treatment requirement:
 - Delayed: care is needed but delaying care will not affect outcome
 - Immediate: emergency care is needed to save life (ABC or antidote)
 - Minimal: minor care by non-physician, admission not needed, quick disposition
 - Expectant: survival unlikely even with optimal treatment, care exceeds available resources
- Decontamination
 - Decontamination lanes should be established prior to medical treatment facility
 - Decontamination teams are non-medical personnel
 - The "clean line" must be strictly adhered to and guarded by armed security
- Evacuation Sorting
 - Urgent (within 2 hr), priority (within 4 hr); routine (within 24 hr)
- Evacuation
 - Identify tertiary medical treatment facilities that patients, once stabilized, can be evacuated to
 - Transportation assets need to be dedicated to medical mission
 - Alternative modes and routes of transportation need to be identified

Сомват

- Medical treatment facilities at each echelon of care render only that care necessary to save life and sufficient to stabilize the patient for evacuation. The goal is to transport the patient to a safe area far away from the combat theater, where definitive medical treatment may be provided.
- A well established, rehearsed evacuation system ensures flow of patients continually to higher levels of care. This prevents medical treatment facilities from filling their available bed space or exhausting their resources.

Bacterial Biological Warfare

- **Anthrax** (JAMA. 2002;287:2236)
 - Signs and symptoms
 - Early: fever, malaise, fatigue, cough, and mild chest discomfort
 - Late: hemorrhagic mediastinitis, severe respiratory distress with dyspnea, stridor, and shock
 - Clinical course: rapid progression to death 1–3 d after late symptoms onset
 - Diagnosis: PCR or ELISA tests early, Positive Gram and Wright stains late, chest X-ray: widen mediastinum (late finding)
 - Treatment: ciprofloxacin 400 mg, IV every 12 hrs, may switch to oral when clinically stable. Treat for 60 d. Alternatives are penicillin or doxycycline
 - Prophylaxis: ciprofloxacin, 500 mg, PO every 12 hrs for 4 wks.
 - Alternative: doxycycline. Vaccine is available.
 - This is not transmitted human-to-human
- **Plague** (JAMA. 2000;283:2281)
 - Signs and symptoms

- Early: swollen glands (bubo), fever, chills, malaise, fatigue, headache, myalgia
- Late: high fever, cough with bloody sputum, pneumonia, sepsis
- Clinical course: fatal within 24 hrs of pneumonia onset if not treated
- Diagnosis: gram negative coccobacillus with bipolar safety pin appearance, Florescent-antibody (FA) or antibody test.
- Treatment: streptomycin, 15 mg/kg, IM, every 12 hrs for 10–14 d.
 - Alternatives are gentamicin, ciprofloxacin, doxycycline
- Prophylaxis: doxycycline
- Transmission: human-to-human is contagious; also rat-to-human via flea
- **Tularemia** (JAMA. 2001;285:2763)
 - Signs and symptoms
 - Early: fever, chills, headache, myalgia, coryza, sore throat
 - Inhalation tularemia presents as a nonspecific febrile illness with pneumonitis developing over days to weeks (much slower than anthrax or plague).
 - Ulceroglandular type: painful ulcerative skin lesions, pneumonia (less common)
 - Typhoidal type: fever, cough, substernal chest pain, pneumonia (more common)
 - Clinical course: begins as nonspecific febrile illness and then over days to weeks progresses to pneumonia leading to respiratory failure, shock and then death
 - Diagnosis: florescent labeled antibody stain by a reference lab. Gram stain reveals tiny pleomorphic gram negative bacilli.
 - Treatment: Streptomycin, 1 gm, IM, every 12 hrs for 10 d.
 - Alternatives are gentamicin, chloramphenicol, ciprofloxacin, doxycycline
 - Prophylaxis: not recommended. Post-exposure treatment if evidence of fever with ciprofloxacin 500 mg, PO, every 12 hr. Alternative: doxycycline.
 - Transmission: human-to-human does not occur

• Q Fever

- Signs and symptoms
 - Early: high fever, chills, headaches, myalgia, headache, malaise, non-productive cough, nausea, vomiting, diarrhea
 - Late: pleuritic chest pain, rales, 50%-60% have abnormal CXR
- Clinical course: lasts up to 2 wks and resolves. Fatality is uncommon
- Diagnosis: blood test for serum antibodies
- Treatment: doxycycline, 100 mg PO × 21 d. Alternatives: macrolides, quinolones.
- Prophylaxis: vaccine is available
- Transmission: human-to-human is rare

Brucellosis

- Sign and symptoms are fever, chills, malaise, headache, myalgia, arthralgia, lumbar back pain, (from osteoarticular infection), mental status changes, depression. Osteoarticular infection leads to lumbar back pain, extremity joint pain, effusion, and immobility
- Diagnosis: Rose-Bengal plate test for rapid screening. Blood or bone marrow culture to confirm diagnosis
- Treatment: doxycycline 100 mg, PO, every 12 hrs for 6 wks.
 - Alternatives are streptomycin, gentamicin, rifampicin, quinolones, or Bactrim
- Prophylaxis: no vaccine
- Transmission: human-to-human is unusual

- **Glanders** and **Melioidosis** (Glanders, Textbook of Military Medicine: Medical Aspects of Biological Warfare. 121–146)
 - Signs and symptoms:
 - Early: fever, chills, sweats, myalgia, headache, pleuritic chest pain, cervical adenopathy, hepatosplenomegaly, papular/pustular rash
 - Late: pneumonia, sepsis
 - Clinical course: fatal if untreated
 - Diagnosis: blood culture. Methylene or Wright stain of exudates reveal small bacilli with safety pin configuration
 - Treatment: doxycycline 100 mg, PO, every 12 hrs with Bactrim, PO for 20 wks plus chloramphenicol, PO, for first 8 wks. For severe cases, ceftazidime at 40 mg/kg, IV, every 8 hrs for 14 d, then switch to mild case oral regimen for remaining 18 wks.
 - Alternatives are ciprofloxacin, imipenem, and meropenem.
 - Prophylaxis: none
 - Transmission: human-to-human via secretions is possible

Viral Biological Warfare

- Viruses that have been weaponized are smallpox and Venezuelan equine encephalitis (VEE).
- **Small Pox** (JAMA. 1999;281:2127)
 - Signs and symptoms
 - Early: fever, chills, malaise, vomiting, headache, backache
 - Late: vesicles, most often on face and extremities
 - Clinical course: up to 40% fatality rate
 - Diagnosis: electron-microscopy of vesicular fluid reveals brick shaped virons, PCR, Guarnieri bodies are seen under light microscopy
 - Treatment: supportive care. There is no clinical evidence demonstrating cidofovir efficacy in humans
 - Prophylaxis: vaccine
 - Transmission: human-to-human is contagious

• Venezuelan Equine Encephalitis

- Signs and symptoms are spiking high fevers, chills, malaise, rigors, headache, photophobia, myalgia in lower back, and legs. Later, sore throat, nausea, vomiting, and diarrhea. Neurological symptoms are unusual in natural VEE but much more common if exposed to an aerosol weapon. If the CNS is affected, then lethargy, somnolence, and confusion occur early followed by seizures, ataxia, paralysis, and coma.
- Clinical course: low fatality rate
- Diagnosis: IgM serology, viral isolation. CSF analysis reveals monocytic leukocytosis and elevated opening pressure
- Treatment: supportive
- Prophylaxis: candidate vaccine is in clinical trial
- Transmission: human-to-human is suspected by not proven

Chemical Warfare

• 6 types of chemical weapons (agents): pulmonary/choking, cyanide/blood, vesicants/blistering, nerve agents, incapacitating agents and riot control. Riot control agents will not be discussed here.

• Hallmark of treatment begins with terminating exposure. This should be done by removing the victim from exposure, placing a gas mask and active cleansing of clothes and skin.

Pulmonary Agents

- The prototypic pulmonary or choking agent is phosgene (CG).
- Detection: odor of "new mown hay or grass," M18A2 and ICAM.
 - M8 and M9 paper and M256A1 tube assays will not detect them.
- Decontamination: fresh air and copious water irrigation
- Triage
 - If seen within 12 hrs of exposure:
 - Immediate: pulmonary edema is present. Early development of pulmonary edema predicts a severe exposure.
 - Such patients need admission to an intensive care unit.
 - Delayed: dyspnea is present. Close monitoring and re-triage every hour.
 - Minimal: known exposure and asymptomatic
 - Expectant: pulmonary edema, cyanosis and hypotension within 6 hrs of exposure will not survive, even with maximal medical therapy. If >6 hrs, then may survive only if intensive care is immediately available
 - If seen beyond 12 hrs of exposure:
 - Immediate: pulmonary edema is present. Such patients need admission to an intensive care unit within a few hours.
 - Delayed: dyspnea is present. Close monitoring and re-triage every 2 hrs. Recovering patients can be discharged in 24 hrs.
 - Minimal: asymptomatic or resolving dyspnea
 - Expectant: hypotension in spite of intensive care treatment
 - Also, patients with pulmonary edema, cyanosis and hypotension.
- Signs and symptoms are eye and airway irritation, dyspnea, chest tightness, and delayed pulmonary edema
- Treatment: terminate exposure and decontaminate
 - Ventilation: an artificial airway should be placed if there is hoarseness or stridor as this portends laryngeal spasm
 - Frequent suctioning, supplemental oxygen, and positive pressure ventilation will likely all be needed. For bronchospasm: theophylline, beta-adrenergic agonists, or parenteral steroids may be used.
 - Cardiovascular: continuous close monitoring of hemodynamic status is paramount as pulmonary edema and positive pressure ventilation may lead to hypotension. Maintain euvolemia and consider applying anti-shock garments
 - Limit activity: Rest is crucial. Even if patient appears well, enforce bed rest to include litter evacuation.
 - Antibiotics: not needed unless clear evidence of infection

Blood agents

- Cyanide is the prototypic blood agent. Among other effects, it binds to iron in cytochrome a3 and methemoglobin.
- Detection: M256A1, M18A2, ICAM; M8 and M9 paper assays will not.
- Decontaminate: skin decontamination is typically not needed. However, if the clothing is wet and

contaminated, then clothing and skin will need decontamination

- Triage:
 - Immediate: convulsions, apnea but circulation is intact. Immediate antidote treatment will be lifesaving.
 - Minimal: exposed but showing minimal symptoms. Antidote may relieve symptoms but is not necessary to save life.
 - Delayed: recovering from exposure or responding to antidote therapy
 - Expectant: apneic with circulatory arrest
- Signs and symptoms: anxiety or apprehension, agitation, vertigo, subjective weakness, nausea, and muscular trembling. This can worsen to coma, seizures, respiratory, and cardiac arrest. Physical signs include severe respiratory distress without cyanosis or, occasionally, cherry red skin. Lab tests are blood cyanide levels, metabolic acidosis, elevated venous blood oxygen content.
- Treatment: Cyanokit^R (Hydroxocobalamin) or Cyanide Antidote Kit^R (contains amyl nitrite pearls, sodium nitrite, and sodium thiosulfate) and supportive care.

Vesicants

- Mustard (HN), Lewisite (L) and phosgene oxime (CX).
- Mustard
 - Mustard's effects are delayed by several minutes as it must dissolve into sweat, tears or extracellular fluid.
 - Detection of HN: M8 and M9 paper assays, M256A1, M18A2 and ICAM
 - Triage
 - Immediate: moderately severe to severe pulmonary effects. Delayed: skin lesion affecting over 50% of body surface area (BSA).
 - Minimal: skin lesions affecting less than 50% BSA
 - Expectant: severe pulmonary effects <6 hrs after exposure.
 - Decontamination: this is the most effective way to treat
 - Signs and symptoms: asymptomatic latent period (hours) followed by erythema and then blistering of skin, conjunctivitis, eye opacity, airway irritation. Nausea and vomiting is usually due to stress reaction and not a direct effect of HN.
 - Treatment: supportive care
 - Patient's body fluids and blister fluid do not contain HN: not vesicants.
- Lewisite
 - Similar to mustard, except Lewisite causes immediate tissue response
- Phosgene oxide
 - Similar to mustard except phosgene oxide causes immediate tissue response but does not blister. Instead, it causes wheal-like lesions

Nerve agents

- There are 5 nerve agents: GA (Tabun), GB (Sarin), GD (Soman), GF, and VX plus pesticides (malathion, parathion, diazinon, trichlorfon, etc.), and herbicides (tribufos, merphos). They are in order of lowest to highest toxicity. These are all organophosphorus cholinesterase inhibitors.
- Detection: M8 and M9 paper assays, M256A1, M18A2, and ICAM will all detect nerve agents.
- Triage
 - Immediate: severe symptoms of seizures, loss of consciousness, difficulty breathing, apnea, flaccid paralysis. Immediate treatment can be life saving.

- Expectant: no blood pressure
- Delayed: recovering from severe exposure following treatment but still requires ventilatory assistance
- Minimal: walking and talking
- Decontamination: necessary
- Signs and symptoms: rhinorrhea is usually the first sign with miosis being the characteristic sign. Low dose: miosis, rhinorrhea, difficulty breathing from bronchoconstriction, nausea, vomiting, muscle fasciculation. Large dose: miosis, diarrhea, loss of consciousness, seizure, apnea, flaccid paralysis, copious secretions.
- Treatment: atropine, 2 mg, IM and pralidoxime chloride (2-PAM), 600 mg, IM Mark 1 kits are these 2 medications packaged together as self administration auto-injectors. The course of therapy is for victims to self-administer a single Mark 1 kit and then seek buddy aid immediately. If, after 10 min, there is no improvement or if the victim is showing signs of severe exposure, then the buddy should administer three Mark 1 kits followed by diazepam, 10 mg, IM
 - After this, additional atropine doses should be given based on resolution of airway secretions and resistance.

Incapacitating agents

- There are 2 incapacitating agents, BZ and Agent 15. Both are atropinic agents
- Detection: none
- Triage:
 - Immediate: cardiopulmonary compromise and severe hyperthermia
 - Physostigmine should be used cautiously in such patients
 - Instead, efforts should focus on ABCs and cooling
 - Delayed: suffering significant central nervous system (CNS) symptoms Physostigmine should be considered
 - Minimal: minor CNS or peripheral nervous system (PNS) symptoms. Will likely not require physostigmine
 - Expectant: severe cardiopulmonary collapse in a situation where treatment and evacuation are not possible
- Decontamination: necessary
- Sign and symptoms: mydriasis, dry mouth, dry skin, decreased level of consciousness, delirium, inattention, impaired memory
- Treatment: physostigmine use is controversial due to its toxicity profile. If used, 45 mcg/kg IM, 30 mcg/kg slow IV infusion (over 4 min or more) or 60 mcg/kg PO (in orange juice as it is bitter). This may be repeated every hour with titration of dose to the patient's mental status. Also, diazepam 2 mg, IV, every 15 min as needed to control agitation. Supportive care.

INFORMED CONSENT, PROCEDURAL STANDARDIZATION AND SAFETY

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Informed Consent

(Clinical ethics: a practical approach to ethical decisions in clinical medicine, McGraw-Hill, 2010;7e:51; Principles of biomedical ethics, Oxford University Press. 2009;6e:99)

- Definition
 - "The willing acceptance of a medical intervention by a patient after adequate disclosure by the physicians of the nature of the intervention, its risks and benefits, and also its alternatives with their risks and benefits"
- Purpose
 - Legal authorization to proceed with a procedure: may be documented on a form, or a note in the chart
 - Promotes shared decision making between physician and patient
 - Preserves patient autonomy to actively authorize a procedure through voluntary consent rather than passive agreement
- Difficulties with Informed Consent in the ICU
 - Physician
 - Use of technical language
 - Uncertain risks and benefits of interventions
 - Limited time
 - Unclear how the patient or proxy is receiving the information, and how to deliver the information to not frighten the patient
 - Deciding if the patient is competent to consent or who serves as surrogate decision maker for the patient
 - Time sensitive procedures which require immediate consent
 - Patient or Proxy (Surrogate Decision-Maker)
 - Limited understanding
 - Selective hearing and comprehension
 - Fear and denial which affect decision making ability
 - Undisclosed conflicts of interest

5 ELEMENTS OF INFORMED CONSENT

- Competence, disclosure, understanding, voluntariness, consent
- Competence
 - Medical context definition: the ability to "understand a therapeutic or research procedure, deliberate regarding its major risks and benefits, and make a decision in light of this deliberation"

- Changes in competence
 - Chronic (dementia)
 - Waxing and waning (delirium) affected by severity of illness, sedatives
- If the patient exhibits delirium but has periods of clarity with consistent decision making, then these decisions should be corroborated with supporting evidence (pre-defined wishes and goals of care, living will) before being implemented.
- Delirium screening (Crit Care Med. 2008;36:94)
 - Two-step approach to obtaining consent: (1) Richmond Agitation—Sedation scale (RASS) and Confusion Assessment Method for the Intensive Care Unit (CAM-ICU), (2) Assessment of competency followed by request for informed consent
- Identifying the surrogate decision-maker if the patient is unable to consent
 - Surrogate or powers of attorney previously appointed by the patient which supersede family members
 - If no surrogate or powers of attorney, then the proxy is state specific, but usually first spouse, parents, children, siblings, then court appointed guardian. Some states have statutes that designate nearest, competent relatives as POA.
- Types of proxy decision making
 - Substituted judgment: when the surrogate or proxy uses knowledge of patient preferences to make medical decisions on behalf of the patient
 - Best interest standard: when the surrogate acts in the best interest of the patient when the patient's preferences are unknown

• Disclosure

- Requirements
 - Stating the patients current diagnosis, medical status, and prognosis if no treatment is provided
 - Explaining risks and benefits of a proposed procedure
 - Offering a professional opinion of alternatives available to the patient
 - Physician recommendation based on clinical judgment
- Ethically should include the level of experience of the provider

• Understanding

- Patient
 - Repeat the proposed procedure
 - Describe the procedure
 - Demonstrate understanding of the risks and benefits
 - Recognize the right to refuse the intervention
- Physician
 - Encourage patient questions and offer answers

Consent

- Two parts
 - Written: documentation of the procedure, risks and benefits, often signed by the patient or their surrogate decision-maker
 - Verbal: consent discussion that leads to the signing of the consent form; discussion contents should be documented by the physician in medical record
- Emergency Situations
 - Medical necessity consent: in life-threatening situations when the patient is unable to consent and a surrogate is unavailable

- Implied consent
 - Assumes the patient would consent if they could in a severe situation as the alternative is death or severe morbidity (e.g., the administration of CPR to a stranger)
 - Protects the physician legally against battery charges

PROCEDURAL STANDARDIZATION

- Procedural standardization is key to improving safety, reducing adverse events, like in the case of central venous catheters where it saved costs and lives. Such standardization efforts are now gradually extending to all common ICU procedures (see Chapters 13 and 39).
- Reducing infection and central venous catheter–related complications (see Chapter 13)

COMMON PROCEDURES

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ENDOTRACHEAL TUBE EXCHANGE

- Indications:
 - Replacement for obstructed ETT or tube with malfunctioning cuff
- Special Considerations:
 - DNR/DNI, difficult airway
- Materials:
 - Intubating instrument (Laryngoscope, Videolaryngoscope, Intubating LMA, Tube changer)
 - Endotracheal tube
 - Stylet (optional)
 - Sedatives/Muscle relaxants (optional)
 - Topical anesthetic (optional)
 - Assistant
 - 10 cc syringe
- Technique (depends on intubation strategy)
 - Position patient supine
 - Prepare rescue medications and suction. Verify working IV if possible
 - Adjust sedation as necessary; may need muscle relaxant once adequate sedation achieved
 - Increase inspired oxygen fraction on ventilator to 100%
 - Intubate
 - Many successful endotracheal tube exchange strategies exist. None are successful all the time. Some sample techniques follow:
 - Direct or videolaryngoscopy
 - This technique is the quickest way to perform tube exchange
 - With the original ETT in place, perform direct laryngoscopy and visualize the vocal cords
 - The laryngoscopist should insert the new endotracheal tube into the mouth and position it parallel to the old tube
 - The assistant should then unfasten the old endotracheal tube, deflate the cuff, and remove it. This way, the patient spends the least time without a secure endotracheal tube and the entire procedure is performed under direct vision
 - Alternatively, a blind tube-changer assisted exchange can be performed
 - An access elbow connector is placed at the end of the endotracheal tube in the circuit to allow placement of the tube changer while the patient is still being ventilated
 - A tube changer is then placed into the old endotracheal tube to a depth sufficient to ensure location in the trachea
 - The old ETT is then removed and a new tube placed over the tube changer. If the new tube does not readily pass through the cords, rotate ETT 180°, apply jaw thrust, or adjust the position of the tube changer

- For particularly difficult airways, use a combination of above techniques. Performing direct laryngoscopy simultaneously with tube changer-assisted exchange allows continuous direct visualization of the exchange and decreases chance of upper airway obstruction preventing passage of the new ETT over the tube changer
 - Verify end-tidal CO₂ and bilateral breath sounds
 - Monitor blood pressure and O₂ saturation
 - Secure endotracheal tube
 - Obtain chest X-ray or perform fiberoptic bronchoscopy to verify tube placement and rule out post-intubation complications
- Complications/Keys to success:
 - Hypoxemia, cardiopulmonary instability, death, esophageal intubation, aspiration, pharyngeal, esophageal, and tracheal perforation, dental/oral injury
 - Most important key to success is anticipatory and contingency planning. When elective, should be performed under optimal conditions and with optimal personnel: consider time of day, nursing/staffing patterns, family availability, etc.
 - Recognize strengths and weaknesses of different visualization strategies

CENTRAL VENOUS CATHETER PLACEMENT (ALSO SEE CHAPTERS 13, 41)

- Indications:
 - Venous access in patients with severe vascular disease
 - Rapid volume resuscitation
 - Central venous pressure monitoring
 - Swan Ganz catheter placement
 - Administration of vasoactive agents or caustic chemotherapy drugs
 - Parental nutrition
- Contraindications:
 - Vascular anomaly
 - Infection at site of catheter insertion
 - Coagulopathy (more for subclavian placement as compression is not possible)
- Complications:
 - Arterial puncture, bleeding, hematoma, infection
 - Pneumothorax (higher incidence with internal jugular or subclavian cannulation)
 - Air embolism, venous thrombosis
- Technique:
 - Discuss the procedure with the patient (if awake)
 - Choose the site of catheter insertion Internal jugular vs. Subclavian vs. Femoral
 - Positioning:
 - If internal jugular approach: position patient in supine, Trendelenburg position, and turn head 30° contralateral to side of catheter insertion. Internal jugular landmarks include the triangle formed by the two heads of the sternocleidomastoid muscle and the medial part of the clavicle. The internal jugular vein is usually located lateral to the carotid artery but may move underneath the carotid, as head rotation increases
 - If subclavian approach lay patient supine (Trendelenburg position is not needed) with small

- towel placed between shoulder blades. The ipsilateral arm should be positioned at the patient's side
- If femoral approach: lay patient supine, and slightly abduct the ipsilateral leg. Palpate the femoral artery (lateral to femoral vein). Needle insertion point: 1–2 cm caudal to inguinal ligament. Leg abduction such as the "frog leg" position (place ipsilateral foot on the contralateral knee) may facilitate exposure of the femoral anatomy
 - Put on mask, cap, gown and sterile gloves
 - Sterilize the skin. ChloraPrep is recommended. The skin should be prepped using a back and forth scrubbing technique to abrade the top layers of the skin and allow the alcohol to penetrate. Note that for the femoral site, care should be taken to not track bacteria from the groin to the line insertion site
 - Drape the patient with the sterile sheet in the kit with the opening over the site of line insertion, and place a second sterile full body drape on the patient over any other exposed areas

For the internal jugular site (see Chapter 41 for ultrasound guided placement):

- If using ultrasound guidance, place the sterile sheath over the ultrasound probe and identify the internal jugular vein. The vein can be distinguished from the artery by Doppler flow pattern, compressibility, position (the vein is superior and lateral to the artery) and pulsatility
- If not using ultrasound guidance, identify the IJ using a 16 gauge finder needle attached to a 5 cc syringe
- Anesthetize the site with subcutaneous local anesthetic
- Using a thin walled hollow needle or catheter-over needle assembly, cannulate the internal jugular vein and insert the guide wire. If using ultrasound, the needle should be introduced so that its contact with the vein can be captured visually by the ultrasound beam. If not using ultrasound, the needle should be aligned with the finder needle so it contacts the vein in approximately the same location

For the subclavian site:

- After palpation of the lateral clavicle, the 16 gauge introducer needle should be inserted 1 cm below and ~3 cm lateral to the mid-point of the clavicle
- Deeper infiltration anesthesia is needed than for internal jugular or femoral sites. Infiltrate the skin and periosteum of the lateral clavicle with lidocaine
- Make contact with the clavicle then "walk" the needle along the clavicle until it passes underneath. Aim needle at the sternal notch, keeping it as parallel to the skin as possible. Once under the clavicle, advance the needle attached to a 5 cc syringe (in many patients the needle may need to be inserted nearly to the hub) while applying continuous negative pressure on the syringe until venous return is achieved

For the femoral site (see Chapter 41 for ultrasound guided placement):

- Palpate the femoral artery with the nondominant hand and anesthetize the site with subcutaneous local anesthetic
- Keeping the non-dominant hand on the femoral artery, advance introducer needle attached to a 5 cc syringe at a 60 degree angle to the skin (cephalad) and advance the needle while aspirating until venous return is achieved
- For all the sites, once the vessel is cannulated, the guide wire should be advanced through the needle to a depth that clearly exceeds the anticipated depth of the cannula. The "J" end of the wire should enter the patient as the "straight" end of the wire may puncture through a vessel during

insertion

- Once the guide wire is placed, its location within the vein should be verified either via ultrasound or manometry. If manometry is used, a catheter should be placed over the wire and into the vessel. The wire should then be removed and the catheter attached to an open piece of IV tubing. Allow the tubing to fill with blood and then raise the free end to evaluate the pressure inside the vessel. If ultrasound is used, the wire should be visualized in the vein
- When the wire location is verified, the insertion site should be dilated and the appropriate catheter inserted. For the subclavian site, care should be taken to verify that the dilator and catheter pass with the wire under the clavicle
- Fasten the catheter to the skin, apply the Biopatch, and dress with transparent adhesive dressing
- Keys to success:
 - Many different successful techniques exist
 - Passing the guide wire can often be as difficult as cannulating the vessel with the needle. If a sufficient length of the guide wire does not pass freely, be extremely careful passing the catheter
 - If the dilator or catheter becomes difficult to pass at any point, verify that the guide wire moves freely to rule out the possibility of a kink in the wire
 - Keep track of the wire at all times to verify that the guide wire does not slip completely into the patient

Pulmonary Artery Catheter Insertion (also see Chapter 2)

- Indications:
 - Direct access to the pulmonary circulation (for delivery of vasodilators or anticoagulants)
 - Diagnosis of complex hemodynamic states including tamponade, and increased pulmonary vascular resistance
 - Pulmonary artery pressure monitoring
 - Cardiac output monitoring
 - Titration of fluid therapy
- Little evidence supports the benefits of PA catheter placement on outcome
- Contraindications:
 - Lack of vascular access
 - Presence of right-sided Ventricular Assist Device (VAD)
 - VSD/ASD
 - Tricuspid regurgitation, presence of right ventricular pacing hardware, or pulmonary stenosis are not contraindications, but may complicate placement
- Keys to success:
 - Many different successful techniques exist for advancing the pulmonary artery catheter. This section will outline some general principles
 - Do not withdraw the catheter while the balloon is inflated as chordal rupture or valve damage may result
 - Do not leave the catheter tip in the RV for any prolonged period. It may cause dysrhythmias and even perforation
 - If the catheter must be inserted excessively far (70+ cm) before a PA tracing is observed, looping may have occurred. The catheter should be withdrawn and readvanced
 - Do not leave the balloon inflated for prolonged periods
 - No evidence exists to favor either continuous advancement or intermittent advancement steps. Both approaches may be successful in specific patients
 - Flat or reverse Trendelenburg position, and tilting the patient left side up may facilitate advancing the catheter to the PA position
 - Be extremely careful "wedging" the catheter. Balloon inflation always involves a risk of pulmonary artery rupture, which is often fatal

ARTERIAL LINE PLACEMENT (SEE CHAPTER 2)

- Indications
 - Beat-to-beat monitoring of blood pressure
 - Assessment of pulse pressure variation
 - a common challenge in arterial line placement is threading of the catheter into the artery which has smaller and thicker muscular walls than a vein; although the needle may easily penetrate the arterial wall, the catheter may not easily pass through the wall
- Contraindications
 - Vascular insufficiency of the arm or hand
- Keys to success
 - A common challenge in arterial line placement is threading of the catheter into the artery which has smaller and thicker muscular walls than a vein; although the needle may easily penetrate the arterial wall, the catheter may not easily pass through the wall

THORACENTESIS

- Indications:
 - Diagnostic (obtain sample for culture, cell count, protein, glucose, triglycerides/cholesterol, cytology/pathology)
 - Therapeutic (Remove air or liquid from the pleural space to improve lung mechanics and work of breathing. Note therapeutic thoracocentesis may be followed by placement of a drainage catheter)
- Contraindications
 - Coagulopathy, noncooperative patient
 - Bullous lung disease (emphysema)
- Materials:
 - Sterile gloves, gown, and drapes. A cap and mask should also be worn
 - Topical sterilizing solution (ChloraPrep[®] is preferred)
 - Local anesthetic, suture, ultrasound machine
 - Assistant (required to stabilize the patient in the sitting position, collect specimens, and hand equipment to the operator)
 - A hollow needle for puncturing the skin and accessing the thoracic cavity and a syringe to identify when the catheter has entered the thoracic cavity. For both diagnostic and therapeutic thoracentesis, a plastic catheter is often mounted over the needle and threaded into the pleural space to reduce damage to the lung from the presence of the sharp needle in the pleural space.
 - Specimen containers to capture the pleural fluid for laboratory analysis
- Technique:
 - Discuss with patient (if awake) and describe procedure
 - Because chest X-rays may not always determine whether sufficient fluid exists to allow successful thoracentesis, ultrasound examination of the thorax may allow an estimate of fluid volume and identify an appropriate insertion site
 - Position the patient. Usually the patient is positioned sitting up with or without the legs dangling off the side of the bed. This position allows pleural fluid to drain to the lowest part of the

thoracic cavity so it can be more easily removed. An assistant may be needed to stabilize the patient in this position

- Identify landmarks for needle placement. To avoid the neurovascular bundle on the underside of each rib, the needle should be "walked off" the superior border of the appropriate rib. If the procedure is performed without ultrasound-guided localization of the fluid collection, or for a needle thoracotomy, the operator should identify the 9th interspace at the mid axillary line and position the needle to enter just over the superior border of the 9th rib. Alternatively, ultrasound may be used to identify the best interspace for loculated or otherwise difficult effusions
- Prep the site. ChloraPrep[®] is preferred, and should be administered in a back and forth, scrubbing motion rather than a concentric "inside out" motion. Drape the area to exclude nonsterile areas
- Anesthetize the insertion site with subcutaneous local anesthetic. Because the needle will contact the rib surface during the "walking off" process, be sure to anesthetize the rib surface as well
- Attach the empty syringe to the thoracentesis needle. Insert the needle perpendicular to the skin until it contacts the surface of the rib below the desired interspace. This step identifies the location of the rib. Then, withdraw the needle slightly, reposition it to still be perpendicular to the skin but more cephalad, and advance again until the rib is contacted. Repeat until the needle slips over the superior border of the rib
- Advance the needle while aspirating with the syringe. Entry into the pleural space should be identified by sudden loss of resistance to aspiration and appearance of fluid in the syringe
- When pleural fluid is aspirated into the syringe, stop advancing the needle. Thread the plastic catheter into the pleural space, remove the needle, and reattach the syringe to the catheter. Remove pleural fluid and/or send for diagnostic studies
- When the procedure is complete, remove the catheter during a period of intrathoracic positive pressure. If the patient is receiving positive pressure ventilation, intrathoracic pressure would be highest during end-inspiration. If the patient is breathing spontaneously, he/she should be instructed to perform a Valsalva maneuver before removing the catheter
- Complications:
 - Infection, hemothorax, pneumothorax, hypotension, reexpansion of pulmonary edema

Needle Thoracostomy

- Indications:
 - Pneumothorax (whether suspected or confirmed) with associated pulmonary or hemodynamic compromise (hypotension, shock, severe dyspnea)
- Contraindications:
 - No absolute contraindications exist
- Materials:
 - 14 gauge or 16 gauge $2-2\frac{1}{2}$ in. needle with cannula
 - 5 cc syringe attached to needle
 - Chlorhexidine skin preps
 - Sterile gauze 4×4 's, tape
- Procedure:
 - On the side of the pneumothorax, proceed with sterile preparation using chlorhexidine skin preps at the second intercostal space, mid-clavicular line

- Insert the needle with attached syringe perpendicular to the chest wall at the superior border of the 3rd rib
- Once the needle makes contact with the 3rd rib, maintain negative pressure on the syringe and walk the needle and catheter over the superior border of the third rib and advance the needle and catheter into the pleural space
- Entry into the pleural space becomes apparent by a "pop" sound, air aspirate into the syringe, or change in resistance
- Once the pleural space is accessed, remove the needle while leaving the cannula in the pleural space
- Secure the cannula with gauze dressing and tape
- Keys to success:
 - Do not reinsert the needle into the cannula since the cannula may be damaged/sheared
 - The procedure should be effective immediately, demonstrated by relief of dyspnea, hypotension, or shock. Air sounds should be audible over side of previous pneumothorax
 - Careful attention to landmarks helps prevent iatrogenic injury

PARACENTESIS

- Indications
 - To obtain fluid for diagnostic analysis
 - To drain fluid from the abdominal cavity
- Contraindications
 - Patient refusal, coagulopathy
 - · Loculated or difficult to access fluid
- Materials
 - Sterile gloves, gown, and drapes. A cap and mask should also be worn
 - Topical sterilizing solution (ChloraPrep is preferred)
 - Local anesthetic, suture
 - Ultrasound machine
 - Assistant (optional) to collect specimens and hand equipment to the operator
 - Paracentesis kit. All kits should have specimen containers to capture the peritoneal fluid for laboratory analysis
- Technique:
 - Verify presence of abdominal fluid. Physical examination is often sufficient, although CT, abdominal X-ray and ultrasound may be useful for complex anatomy
 - Supine position or head/back slightly elevated to allow intraabdominal fluid to collect in one place. Occasionally, a lateral position may be used
 - If large volume paracentesis is planned, blood pressure and pulse oximetry monitoring
 - Identify landmarks for needle placement. Avoid the liver and any visible blood vessels. If the procedure is performed without ultrasound-guided localization of the fluid collection, the periumbilical area is usually chosen. Alternatively, ultrasound may be used to identify the best entry site for loculated or otherwise difficult effusions
 - Prep the site. ChloraPrep[®] is preferred, and should be administered in a back and forth, scrubbing motion rather than a concentric "inside out" motion. Drape the area to exclude nonsterile areas

- Anesthetize the insertion site with subcutaneous local anesthetic. Aspirate during needle movement. If ascites fluid is withdrawn during local anesthetic infiltration, withdraw the needle until fluid drainage stops
- When the needle enters the peritoneal cavity, thread the plastic catheter and remove the needle. Peritoneal fluid may be withdrawn using either a syringe or by attaching the catheter to a vacuum bottle

NASOGASTRIC AND DOBBHOFF TUBE PLACEMENT

- Indications:
 - Administration of feeds and oral medications
- Nasogastric tubes:
 - Decompression of gastrointestinal tract when ileus or bowel obstruction present
 - Suction and removal of gastric contents (i.e., overdose ingestion)
 - Lavage and suction for evaluation of gastrointestinal bleeding, or for active internal warming or cooling of a patient
 - Administration of activated charcoal
- Dobbhoff tubes:
 - Safer administration of feeds and oral medications during operating room procedures potentially lowering the risk of aspiration since the tube can be placed distal to the pyloric sphincter in the proximal duodenum
- Contraindications:
 - Maxillofacial trauma
 - Esophageal abnormalities such as stricture
 - Abnormal anatomy (esophagectomy, gastric bypass)
 - Caustic ingestion
 - Nasogastric tube: inability to protect the airway (if the patient has high residuals from gastric feeds, these feeds may be aspirated)
- Materials:
 - Nasogastric or Dobbhoff tube, lubricant, 60 cc syringe, stethoscope, tape, glass of water, 10 cc saline
- Procedure
 - Sitting position if awake and not intubated with the neck flexed; if intubated and sedated, lay the patient flat in bed and place one hand under the patient's head to flex the neck (when flexing the neck be careful that the endotracheal tube does not migrate into the right mainstem bronchus)
 - Measure the tube from the ear to the nose to the xiphoid; this is how far the tube should be inserted; the Dobbhoff tube has markings and is usually inserted to ~65 cm
 - Generously lubricate the tip of the tube
 - If inserting a Dobbhoff tube, flush the tube first with 10 cc of saline, keeping the wire in place
 - Insert the tube through the nares (for the Dobbhoff, keeping the wire in the tube during insertion) parallel to the floor of the nares, not angled cephalad or caudad
 - If resistance is met and if the patient is not intubated and gags, ask them to start drinking water and with each swallow slowly advance the tube until the proper length of the tube is inserted
 - Resistance is often met at the gastroesophageal junction, and at the pylorus as the Dobbhoff is

supposed to pass the pylorus into the proximal duodenum

- Secure the tube to the nose with tape
- Note: many institutions now require direct visualization of the passing of the Dobhoff tubes into the esophagus (and not the trachea as it can cause severe lung damage if it passes to the lung). These visualization techniques can use X-ray, direct laryngoscopy or fiberoptic bronchoscopy
- Nasogastric tube confirmation
 - Confirm placement by injecting the tube with the 60 cc syringe filled with air while listening over the gastrum with the stethoscope hear a rush of air/bubbles
 - When connected to suction, gastric contents should return
- Confirm placement with chest X-ray
- Dobbhoff tube confirmation
 - It is prudent that the operators use direct visualization techniques during placement and assure that the Dubhoff tube is NOT placed into the trachea or lungs
 - The Dobbhoff should be below the diaphragm and should cross the midline to be properly placed in the duodenum
 - Once the Dobbhoff placement is confirmed the wire may be removed
 - The Dobbhoff may be used whether it is intragastric or in the proximal duodenum
 - The risk of aspiration with Dobbhoff placement is potentially lower when it is placed past the pylorus in the duodenum
- Complications (Acute and Chronic)
 - Endotracheal placement (patient will have difficulty speaking, or lower tidal volumes on ventilator)
 - Intracerebral placement (leakage of cerebrospinal fluid from perforated cribriform plate)
 - Pneumothorax, aspiration
 - Bleeding (epistaxis), esophageal perforation
 - Sinusitis, ulceration
- Keys to Success
 - Insert tube parallel to the floor of the nares
 - Do not force tube placement when resistance is met
 - Removing the tube a few centimeters and twisting the tube gently may help with the placement; use generous lubrication
 - Always flush a Dobbhoff with the wire in place before inserting the Dobbhoff
 - Only remove the wire from the Dobbhoff once the positioning is confirmed on an abdominal film or by fluoroscopy
 - Never re-insert the Dobbhoff wire after it has been pulled

LUMBAR PUNCTURE

- Indications:
 - Obtain opening pressure
 - CSF drainage for high intracranial pressure (if risk of herniation is low)
 - CSF sampling for diagnostic
- Contraindications:
 - High intracranial pressure and risk of cerebral herniation

- Coagulopathy/thrombocytopenia (controversial)
- Local infection at site of lumbar puncture
- Anticoagulated patient
- Fused lumbar vertebrae
- Patient refusal
- Materials:
 - Lumbar puncture kit, sterile gloves and drape, mask/cap
- Technique:
 - Discuss procedure with patient (if awake)
 - Position patient either sitting or lateral. If sitting place chin to chest, with arms resting on a table to maximally flex the back. If lateral, bring chin to chest and knees to chest (fetal position)
 - Prep the site. ChloraPrep® is preferred, and should be administered in a 30 sec back and forth, scrubbing motion rather than a concentric "inside out" motion. Drape the area to exclude nonsterile areas
 - Identify interspaces. The interspace associated with the top of the iliac crest is usually L4–L5 interspace. Choose this interspace or one interspace up (L3–L4) for the lumbar puncture, whichever feels more open, more space between the spinous processes
 - Anesthetize the skin via subcutaneous infiltration with local anesthetic. Infiltration below the subcutaneous layer may be needed as the dura is 3–5 cm below the skin in most patients. Reidentify the space between the spinous processes and insert both the spinal needle and introducer as a unit, with bevel facing cephalad. The spinal needle and introducer will pass through the skin, subcutaneous tissue, supraspinous ligament, and interspinous ligament. A greater resistance will be felt by the operator as the needle and introducer move through the ligamentum flavum. The needle should be directed perpendicular to the skin, or aimed slightly cephalad in alignment with the spinous processes
 - Although not universal, a change in resistance may occur when the introducer/spinal needle passes through the dura and into the spinal canal. Remove the spinal needle while holding the introducer steady
 - Measure the opening pressure. This is usually done by attaching the introducer to a column manometer and marking the height of the CSF after it reaches equilibrium
 - Collect CSF for diagnostics The amount of the CSF collection can vary depending on the tests being ordered
 - When CSF collection is complete, place the introducer into the spinal needle and remove as one unit
 - Wipe off back with gauze and water, place gauze dressing over site of lumbar puncture, remove drape, reposition patient comfortably in bed
 - The patient should be ordered a brief, 30 min bed rest following the procedure
- Complications:
 - Bleeding/hematoma, infection/abscess/meningitis, headache, paralysis

URINARY CATHETER (FOLEY) PLACEMENT

- Indications:
 - Drain bladder contents/decompress the bladder, obtain urine specimen, identify GU bleeding,

monitor volume status/renal perfusion by evaluating urine output, treat bladder outlet obstruction, treat urinary retention, bladder irrigation

- Obtain urine specimen
- Identify GU bleeding
- Monitor volume status/renal perfusion by evaluating urine output
- Treat bladder outlet obstruction
- Treat urinary retention
- Bladder irrigation
- Contraindications:
 - Urethral trauma, blood present at the urethral meatus, pelvic fracture, scrotal hematoma, high riding prostate, inadvertent vaginal insertion
- Procedure:
 - Discuss the procedure with the patient (if awake)
 - Place patient in supine position, legs abducted, feet together
 - Open the Foley catheter kit
 - Put on mask/sterile gloves
 - Coat cotton swabs with sterile Betadine solution
 - For the female patient: use non-dominant hand to separate labia
 - For the male patient: use the non-dominant hand to hold the penis
 - With the dominant hand use forceps to hold sterile coated cotton swabs and cleanse the periurethral space (inner to outer, anterior to posterior) with one swipe per swab
 - Discard swabs away from sterile field; apply sterile drape
 - Check the catheter balloon for patency by injecting 10 cc of saline into the balloon and then aspirating back the 10 cc saline into the syringe to the balloon is deflated for Foley placement
 - Place generous lubrication over distal ~3 cm of Foley catheter
 - For the female patient: continue to spread the labia with the non-dominant hand- with the dominant hand hold Foley catheter and gently insert 1–2 in. beyond the point where urine is returned
 - For the male patient: hold the penis perpendicular to the patient's body with the non-dominant hand using upward traction with the dominant hand insert the Foley 1–2 in. beyond the point urine is returned
 - Inflate the balloon using a set amount of sterile water (usually ~10 cc)
 - With a gentle tug, pull the catheter back until the inflated balloon sits against the bladder neck
 - Connect the drainage system to the catheter
 - Secure the catheter to the thigh making sure to prevent tension on the tubing
 - The drainage bag should be below the level of the bladder
- Complications/keys to success:
 - If prostatic hypertrophy present, or urethral stricture, the insertion of the catheter may be difficult and a urology consult is indicated
 - Tissue trauma, bleeding, infection are possible complications
 - If unable to pass the catheter, a smaller size may be needed

BEDSIDE SURGICAL PROCEDURES

Oveys Mansuri, MD • Lashonda Williams, MD • Selwyn O. Rogers, Jr., MD, MPH

These bedside surgical procedures should be performed by surgeons and assisted by critical care personnel.

Bedside Tracheostomy (Crit Care. 2006;10:202; Crit Care. 2006;10:R55)

- Indications
 - Respiratory failure and need for prolonged intubation
 - Airway protection
 - Access for pulmonary toilet
- Contraindications/Considerations
 - Infection at site
 - Coagulopathy
 - Anatomic variation (e.g., short neck)
 - High ventilatory requirement (e.g., PEEP > 10)
- Materials
 - Bronchoscope
 - Percutaneous tracheostomy kit (including: scalpel, needle, guidewire, dilators, and tracheostomy)
- Technique
 - Position patient supine with neck extended
 - Administer appropriate sedation
 - Bronchoscopy through endotracheal tube with identification of tracheal rings
 - Apply local anesthetic
 - Carefully withdraw endotracheal tube partially while maintaining bronchoscopic visualization
 - Insert needle along midline into trachea under direct visualization by bronchoscopy
 - Advance guidewire through needle and then remove needle
 - Perform serial dilations over guidewire maintaining bronchoscopic visualization or use single dilator system
 - Insert tracheostomy tube, confirm position, and secure tube
 - Obtain CXR to verify placement and rule out post-procedure complications
- Complications/Keys to Success
 - Bleeding: apply pressure if uncontrolled, then proceed to OR for exploration
 - Pneumothorax: possible need for tube thoracostomy
 - Loss of airway: abandon procedure and regain airway by reintubation
 - Tracheo-arterial/esophageal fistula: rare complication that requires appropriate surgical consultation

Bedside PEG (Percutaneous Endoscopic Gastrostomy) (Nutr Clin Pract. 2005;20(6):607; Surg Endosc. V23, N11, 2580; Eur Arch Otorhinolaryngol. 2010, Nov 3)

- Indications
 - Need for long-term enteral access

- Contraindications/Considerations
 - Infection on abdominal wall
 - Coagulopathy
 - Prior abdominal surgery
 - Anatomic variation and/or disease (tumor, varices, ulcer, or ascites)
- Materials
 - Endoscope
 - Percutaneous gastrostomy kit (including: scalpel, needle, guidewire, dilators, and gastrostomy tube)
- Technique
 - Endoscope stomach and insufflate stomach
 - Use endoscope to transilluminate abdominal wall
 - Apply local anesthetic to site of maximal illumination
 - Introduce needle under endoscopic visualization
 - Pull technique
 - Guidewire placed through introducer
 - Pulled out through mouth using endoscope
 - Attach to PEG tube
 - PEG tube then pulled into stomach and through abdominal wall
 - PEG tube secured noting position
 - Repeat endoscopy to confirm appropriate placement and rule out complications
- Complications/Keys to Success
 - Do not proceed with PEG tube placement if inadequate transillumination
 - Bleeding
 - Infection
 - Bowel perforation
 - Device malposition
 - Gastrocolocutaneous fistulas

Bedside Diagnostic Laparoscopy (Curr Opin in Crit Care. 2006;12(4):333–339; Surgery. 2002;131:491–496; Crit Care. 2009;13:R25)

- Indications
 - Abdominal pain or fever without obvious etiology in the presence of sepsis without clear indication for laparotomy
 - Metabolic acidosis without etiology
 - Multi-organ system failure without explanation
 - Critically ill patients with possible abdominal pathology who are in need of additional diagnostic study and not immediately appropriate for laparotomy or unstable for transport to operating room or abdominal CT
- Contraindications/Considerations
 - Indication for formal exploratory laparotomy (bedside laparoscopy is not a substitute for patients requiring formal exploration)
 - Coagulopathy
 - Abdominal compartment syndrome (ACS)
 - Extensive prior abdominal surgery

- Abdominal wall infection
- Morbid obesity (relative contraindication)
- Physiology refractory to treatment of intra-abdominal process
- Materials
 - Personnel: surgeon, assistant surgeon, anesthesiologist, scrub nurse, circulator, and critical care nurse
 - Standard laparoscopy tower
 - Sterile drapes, gowns, gloves, set of sterile surgical instruments for diagnostic laparoscopy
- Technique
 - Strict adherence to universal precautions and routine OR sterile protocols
 - General anesthesia administered by anesthesiologist
 - Peritoneal access can be achieved by various methods including Veress needle, Visiport, or open technique
 - Pneumoperitoneum should be achieved by inflating the abdominal cavity with carbon dioxide to a pressure of 8–15 mm Hg.
 - Laparoscopic exploration of the abdomen should be performed with careful attention to standard safe practices
 - Port sites should be appropriately closed
- Complications/Keys to Success
 - Veress needle and/or trocar injury to solid organ, hollow viscous, or vascular structure
 - Hemodynamic instability secondary to carbon dioxide insufflation
 - Recognize limitations of laparoscopy and be prepared for complications requiring conversion to open procedures in the ICU setting and/or aborting the procedure

Bedside Decompressive Laparotomies (Acute Care Surgery: Principles and Practice, Ch 8, p. 118; 2007; Current Surgical Therapy. 9e. p. 970;2008; The Trauma Manual: Trauma and Acute Care Surgery. 3e. Ch 29, p. 293;2008; Am J Crit Care. 2003;12:367)

- Indications
 - ACS
 - Washout/pack removal (bedside laparotomy)
- Contraindications/Considerations
 - Abdominal operations requiring
 - Intestinal anastomoses
 - Ostomy creation
 - Definitive hemorrhage control
 - Coagulopathy
- Materials
 - Personnel: surgeon, assistant surgeon, anesthesiologist, scrub nurse, circulator, and critical care nurse
 - Sterile drapes, gowns, gloves, set of sterile surgical instruments for laparotomy, variety of suture material
- Technique
 - Prior to incision:
 - Strict adherence to universal precautions and routine OR protocols
 - General anesthesia administered by anesthesiologist

- Patient should be adequately resuscitated with reliable access to ensure large volume replacement if necessary
- Prep and drape in usual sterile fashion
- Enter the abdomen:
 - Make an incision from the xiphoid process to the symphysis pubis
 - Incision should be taken down to the level of the fascia, and the fascia then carefully opened
 - Careful attention should be paid to the patients respiratory and hemodynamic parameters at the time of release of the fascia
 - Routine exploration of the abdomen should be performed at this time
- Temporary abdominal closure:
 - Insert large sterile towel and cover on both sides with Ioban (3M) sterile adhesive drape
 - Tuck below the fascia and overlying the bowel and omentum
 - Two JP drains should be placed over the Ioban and cover with laparotomy pads
 - Cover with an additional large piece of Ioban (3M) drape
 - Apply suction to the system
- Complications/Keys to Success
 - Plan to return for re-exploration and washout in 24–48 hrs
 - Recurrent ACS
 - Infection, that is, abscess or other infected fluid collection
 - Cardiovascular collapse at time of decompression that will require aggressive volume resuscitation

Debridement (J Vasc Surg. 2010;52:31S; Acute Care Surgery: Principles and Practice. Ch 11, p. 172, 2007)

- Indications
 - Infected or necrotic wounds
 - Chronic non-healing wounds in the absence of ischemia
- Contraindications/Considerations
 - Underlying vascular disease with associated gangrene
 - Coagulopathy
- Materials
 - Local anesthetic
 - Scalpel blades
 - Hemostat, clamp, forceps, curved mayo scissors, electrocautery (if available)
 - Gauze, dressing supplies, and tape
 - Sterile saline
- Technique
 - Place disposable, absorbable drapes under and around area of procedure to minimize contamination of linens
 - Prep and drape area in usual fashion
 - Apply local anesthetic to area or provide parenteral sedation (if needed)
 - Make incision in the area most inflamed, tender, or indurated
 - Incise and assess for necrotizing soft tissue infection
 - Excise all necrotic tissue using scalpel or curved mayo scissors
 - Evaluate wound for hemostasis and any remaining devitalized tissue
 - Wounds should be dressed in sterile gauze or bandages moistened with sterile saline

- Complications/Keys to Success
 - Do not proceed with any debridement no matter how minor unless you understand and appreciate the anatomy
 - Do not hesitate to perform any extensive debridement procedure in the operating room if the patient is stable and there is concern for safety
 - Return to wound within 24 hrs to re-assess need for additional debridement
 - Be careful not to miss areas of infected or necrotic tissue and/or fluid collections
 - Be concerned about bleeding, vascular and/or nerve injury
 - When infection is documented or suspected, it is imperative to start immediate treatment with broad-spectrum antibiotics, especially in cases of necrotizing fasciitis
 - Obtain appropriate wound care and nutritional consult to optimize wound healing and recovery

Emergent Thoracotomy (ATOM – Advanced Trauma Operative Management. p. 358, 2004; Trauma Manual. 4e. Ch 9, p. 91, 2003; World J Emer Surg. 2006;1:4; The Trauma Manual: Trauma and Acute Care Surgery. 3e. Ch 25, p. 230, 2008; World J Surg. 2008;32:604; Manual of Common Bedside Surgical Procedures. 2e. Ch 4, p. 138, 2000)

- Indications
 - Witnessed penetrating trauma <15 min of prehospital CPR
 - Witnessed blunt trauma <5 min of prehospital CPR
 - Post injury hypotension (SBP \leq 60): cardiac tamponade, hemorrhage, air embolus
 - ATLS
 - Qualified surgeon must be present at the time of the patient's arrival to determine the need and potential for success of a resuscitative thoracotomy in the ED
 - Penetrating trauma + prehospital CPR + no signs of life + no cardiac electrical activity = no indication for resuscitative thoracotomy
- Contraindications/Considerations
 - Penetrating trauma: >15 min CPR and no signs of life
 - Blunt trauma: >5 min CPR and no signs of life or asystole
 - Emergent thoracotomy for blunt trauma and cardiac arrest is rarely effective
 - Signs of life: reactive pupils, spontaneous movement, organized ECG activity
 - Relative contraindication: prior thoracotomy/dense pleural adhesions
- Materials
 - Sterile prep: chlorhexidine/betadine
 - Sterile gloves and towels
 - #10 blade and scalpel
 - Functional suction apparatus
 - Resuscitative thoracotomy kit: chest wall retractor (Finochietto), mayo scissors, metzenbaum scissors, smooth forceps, toothed forceps, aortic/vascular clamp
- Technique
 - Intubated with endotracheal tube and appropriate IV access
 - Supine position with LEFT arm above the head and wide prep
 - Thoracotomy, pericardiotomy, and cardiac repair
 - Identify LEFT 5th intercostal space (in females displace breast cephalad)
 - Incision from lateral edge of sternum to latissimus dorse with #10 scalpel
 - Divide intercostal muscles and parietal pleura along superior margin of rib using heavy scissors
 - Place rib retractor with the handle directed inferiorly toward the axilla and T-bar posteriorly

- near the bed
- Open the pericardium anterior to the phrenic nerve
- Any blood clots should be evacuated and bleeding sites controlled with digital pressure
- Cardiac repair/cardiac function
 - Beating heart: delay repair until resuscitation complete
 - Non-beating heart (see cardiac arrest below)
 - Repair done prior to defibrillation
 - Use 3-0 nonabsorbable horizontal mattress sutures or running (Teflon pledgets routinely on RIGHT heart, selectively on LEFT)
 - Balloon catheter occlusion: use selectively, may increase size of hole
- Cardiac arrest: may occur during emergent thoracotomy
 - Bimanual internal massage should be performed (do not use one hand)
 - Internal defibrillation first at 20 J followed by 30 J
 - Aortic occlusion via cross-clamp
 - Elevate the left lung anteriorly and superiorly
 - Incise the mediastinal pleura and bluntly separate aorta from the esophagus anteriorly and prevertebral fascia posteriorly
 - Cross-clamp inferior to left pulmonary hilum
 - If unable to visualize or place clamp safely, may digitally occlude aorta against spine
- Complications/Keys to Success
 - Emergent thoracotomy patients must be eventually taken to OR for definitive evaluation of injuries and repair, and their ATLS work-up completed as appropriate
 - Poor exposure: make incision as wide as possible
 - Internal mammary artery laceration: should be repaired in the OR
 - Esophageal injury (most likely to occur during aortic cross-clamp)
 - When performing ventricular repair, careful attention must be paid to coronary vessels (suggested: vertical mattress sutures)
 - Chest wall infection, intra-thoracic infection, that is, empyema
 - Recurrent bleeding
 - Risks to health care providers: be mindful of sharps and exposure to bodily fluids, universal precautions including eye protection are a must

Chest Tube/Tube Thoracostomy (see Chapter 39)

Tunneled Central Venous Catheter Removal (*Radiology*. 2001;219:651–654; *British Journal of Radiology*. 2005;78:147–149)

- Indications
 - Infected catheters or catheter no longer needed
- Contraindications/Considerations
 - Uncontrollable bleeding diathesis
- Materials
 - Scalpel #10 or #15 blade
 - Hemostats
 - Forceps
 - Mayo scissors
 - Nonabsorbable suture
 - Local anesthetic
 - Surgical gauze
 - Sterile saline
- Technique
 - Prep and drape the surgical field in the standard surgical fashion
 - If the patient is obese or edematous, the ultrasound machine may be used for localizing the cuff of the catheter
 - Anesthetize the skin and surrounding tissues overlying the cuff of the catheter
 - Make a skin incision overlying the cuff of the catheter
 - Dissect the cuff of the catheter free from the underlying skin and soft tissues
 - Once the cuff of the catheter is free, it should be removed as a single unit without any difficulty
 - Ensure adequate hemostasis is present
 - Close the skin with interrupted nonabsorbable sutures
- Complications/Keys to Success
 - Retention of the cuff of the catheter
 - Partial removal of the catheter
 - if the catheter does not remove easily after adequate dissection, abort the procedure

Wound V.A.C. Changes

(http://www.kci1.com/KCI1/vacapplicationvideosandguides)

- Indications
 - Skin grafts and local flaps
 - Diabetic ulcers
 - Pressure ulcers
 - Acute and/or subacute wounds
 - Traumatic wounds
- Contraindications
 - Excessive pain uncontrollable with intravenous medications
 - Coagulopathy
 - Wound with necrotic and/or nonviable tissue
 - · Infected wound

- Untreated osteomyelitis
- Exposed arteries, veins, or nerves
- Malignancy in wound
- Materials
 - Appropriately sized V.A.C. sponge, drapes and Sensa T.R.A.C. pad
 - Sterile saline
 - Sterile gloves, surgical gown, and eyewear
 - Surgical gauze
- Technique
 - Turn off the V.A.C. machine prior to removing the old dressing
 - Gently remove the old dressing
 - Irrigate the wound with normal saline
 - Cut and shape the foam dressing to fill the entire width and depth of the wound prior to placing it on the wound
 - Fill in any sinus tracts or cavities within the wound with the foam dressing
 - Size and trim the clear plastic dressing to cover the wound and \sim 2–3 cm of the surrounding skin circumferentially
 - Cut a small hole ~2 cm in size in the clear plastic dressing before it is applied to the foam sponge
 - Remove the backing from the Sensa T.R.A.C. pad and place it directly over the opening in the drape
 - Connect the Sensa T.R.A.C. tubing to the canister tubing
 - Set adequate pressure to 125 mm Hg and check the system for any leaks
- Complications/Keys to Success
 - Seal any leaks with the excess V.A.C. drapes
 - If the foam sponge does not remove easily, apply saline to the sponge prior to removal

Burn Escharotomies (J Burn Care Res. 2009;30:759; Acute Care Surgery: Principles and Practice. 2007:125)

- Indications
 - Sudden onset of neurological symptoms in full thickness extremity burns
 - Absence of pulses or decreasing doppler signals
 - Hypoxia, increased work of breathing, and increased peak inspiratory pressures
- Contraindications/Considerations
 - Coagulopathy
- Materials
 - Bovie electrocautery
 - Scalpel #10 blade
 - Grounding pad
 - Surgical sponges
 - Surgical gowns and sterile gloves
- Technique
 - Set the bovie electrocautery to coagulation and place the grounding pad on the patient
 - With extremity eschars, incise the eschar down to the fascia from the upper to lower limit of the burn wound in the midlateral line of the involved extremity
 - Reassess circulatory status of the limb
 - If distal flow is not restored, perform an escharotomy in the midmedial line of the involved limb

- With truncal escharotomies, incise the eschar in the anterior axillary lines bilaterally
- If the abdomen is involved, an incision should be made along the costal margin in a curvilinear fashion joining the bilateral anterior axillary line incisions
- Complications
 - Injury to underlying tendons and neurovascular bundles
 - Inadequate escharotomies leading to ischemic injury requiring fasciotomies
 - Bleeding

Pericardiocentesis (Crit Care Clin. 1992;8:699)

- Indications
 - Pericardial tamponade
- Contraindications/Considerations
 - Uncorrected bleeding diatheses in non-emergent setting
 - Always have cardiac surgical backup
- Materials
 - 16–21 gauge spinal needle
 - 60 cc syringe
 - Continuous ECG monitoring
 - Systemic arterial pressure monitoring
 - Personnel and equipment required for emergency intubation and cardiac resuscitation
 - 1% lidocaine with epinephrine
- Technique
 - Place patient in supine or semi recumbent position
 - Infiltrate local anesthesia to the left of the xiphoid tip
 - Attach a 16–21 gauge cardiac or spinal needle with a short bevel to a 20 cc syringe filled with local anesthetic
 - Attach an alligator clip lead to a V lead of the ECG monitor on the hub of the needle
 - Introduce the tip of the needle between the xiphoid and left costal margin aiming toward the left shoulder at a 45 degree angle to the abdominal wall
 - Carefully advance the needle while applying constant negative pressure until a return of fluid is visualized
 - Inject small volumes of local anesthetic into the deeper tissues as the needle is being advanced
 - If injury pattern is seen on the ECG such as ST changes or pulsations transmitted through the needle, the needle should be withdrawn a few millimeters and readvanced more medially
 - Remove approximately 50 ml of bloody fluid
 - Place a soft catheter over guidewire through the needle for continuous drainage
- Complications
 - Atrial or ventricular puncture
 - Atrial or ventricular laceration
 - Cardiac arrhythmias
 - Vasovagal reaction
 - Pneumothorax
 - Gastric or bowel perforation
 - Acute pulmonary edema

Intracranial Pressure Monitors/External Ventricular Drain Placement (Schmidek and Sweet's Operative Neurosurgical Techniques: Indications, Methods and Results, V1, 5e. 2006:35; J Neurosurg. 1980; 53:662; Neurocrit Care. 2009;10:241; Operative Neurosurgery. 2008;1:S162)

- Indications
 - Primary or secondary hydrocephalus secondary to subarachnoid hemorrhage
 - Traumatic brain Injury with a Glasgow Coma Scale <8 and abnormal Head CT
 - Refractory intracranial hypertension
- Contraindications
 - Uncorrected bleeding diathesis
- Materials
 - 1% Lidocaine with epinephrine
 - Scalpel #10 or 15 blade
 - Manual twist drill
 - 18 Gauge needle
 - Commercially available ICP monitor or EVD kit
 - Sterile gloves and gown
 - Sterile drapes, towels, and gauze
 - Sterile saline solution
 - External drainage collection kit
- Technique
 - Place the patient in the supine position
 - Shave the patient's head widely
 - Prep and drape the shaved area of the scalp
 - Infiltrate the skin with local anesthetic
 - The catheter is normally placed on the nondominant hemisphere unless the ventricle is collapsed
 - Mark the midline
 - Make an incision from skin to bone at a point 10 cm back from the naison and 3 cm lateral to the midline
 - Use the manual twist or power drill to penetrate the cranium
 - Remove the bony fragments
 - Insert a probe to ensure that the drill has completely penetrated the skull
 - Use a 18 guage needle to puncture the dura
 - If a ventricular drain is placed, insert the ventriculostomy catheter through the burr hole aiming at the foramen of Monro
 - Aim the catheter toward the ipsilateral medial canthus in a mediolateral plane and ipsilateral tragus in the anteroposterior plane
 - Pass the catheter to a depth of \sim 55–60 cm from the outer table of the skull
 - Tunnel the catheter through the skin through a separate stab incision
 - Secure the catheter to external tubing
 - If an ICP monitor is placed, use the same steps for the skin incision and entering the skull except
 - Open the dura with a small stylet
 - Screw in a fixation bolt to hold the parenchymal catheter into place
 - Pass the catheter 1–2 cm into the parenchyma
 - Secure the bolt in place
 - Ensure that appropriate waveforms are visualized

- Secure the catheter into place with nonabsorbable suture, if needed
- Apply a sterile dressing to the site
- Complications
 - Intraparenchymal, interventricular, or subdural hemorrhage
 - Infection (ventriculitis, meningitis, etc.)
 - Catheter-related infection
 - Catheter malfunction
 - Catheter malposition

Suprapubic Cystostomy (Clinical Procedures in Emergency Medicine. 5e. 2007:1028)

- Indications
 - Ureteral structure
 - Complex prostatic diseases
 - Suspected ureteral injury
- Contraindications/Considerations
 - Non definable bladder
 - Prior lower abdominal surgery/radiation to abdominal wall
 - Bleeding diathesis
- Materials
 - · Local anesthesia
 - 22 Gauge Spinal Needle
 - Percutaneous suprapubic cystostomy kit
 - Surgical drapes
 - Surgical gowns, sterile gloves, hat and eye protection
 - Scalpel #10 blade
- Technique
 - Shave the lower abdomen and then prep the lower abdominal skin widely with skin prep
 - Drape the lower abdominal widely with the drapes below the umbilicus and pubic symphysis
 - Using a spinal needle, anesthetize the skin and subcutaneous tissues 2–3 cm above the pubic symphysis
 - Next, anesthetize the underlying rectus abdominis fascia
 - Identify the bladder by inserting the needle into the bladder at a 10–20 degree angle aiming the needle towards the pelvis
 - Aspirate continuously while the needle is advancing
 - Once urine is seen, remove the syringe and insert the guidewire through the needle
 - Remove the needle and make a stable incision posterior to the guidewire
 - Advance the dilator and its sheath over the guidewire
 - Remove the guidewire and the dilator leaving the sheath in place and pass the foley balloon catheter through the sheath
 - Aspirate urine to confirm that the catheter is within the bladder
 - Remove the sheath
 - Fill the foley catheter balloon with 10 ml of saline and withdraw the catheter until it is positioned at the cystostomy site
 - Cleanse the wound and dress it with a dry dressing
- Complications

Bowel perforation, hematuria, ureteral catherization, obstruction of tubing, tubing coming out, intraperitoneal extravasation, extraperitoneal extravasation							

ULTRASOUND-GUIDED THERAPY AND PROCEDURES

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ECHOCARDIOGRAPHY IN THE MANAGEMENT OF SHOCK

Pericardial Tamponade Temponade Effusion physiology Akinetic/ Global or Acute LV Failure hypokinetic **RWMA** LV PARASTERNAL Signs of /SUBCOSTAL/ Pressure or Acute RV Hypokinetic RV APICAL Volume dysfunction overload IVC Collapsibility, Hypovolemia Small Aortic flow variation hyperdynamic Sepsis/SAM/ heart Tension Pneumothorax

Figure 1. Shock Algorithm for Echocardiography

Echocardiographic Approach to Tamponade

- Demonstration of pericardial fluid (have to distinguish between pericardial and pleural fluid)
 - Localized or circumferential echo-free space (echolucency) surrounding the heart
 - Limited by parietal pericardium
- Demonstration of tamponade physiology
 - Right atrial systolic collapse (60% specificity and sensitivity)
 - Fluid accumulation in pericardial sac
 - RA thin walled RA with low intracavitary pressures
 - Collapse-lowest pressure in end diastole
 - Right ventricular diastolic collapse (Intrapericardial pressure > RV pressure)
 - Fluid accumulation in the pericardium
 - RV lowest pressure in diastole
 - Collapse starting in the RV outflow tract
 - 60% sensitive and 90% specific
- Respiratory variation in transmitral flow (Intrathoracic pressure → intrapericardial pressure → PCWP-LADP)
 - Diastolic filling gradient

- Tamponade-fluid isolates pericardium
- Decrease in inspiratory filling
 - AMitral inflow
- Decrease in transmitral flow
- Ventricular interdependence
- Inferior vena cava plethora
 - Increased RA pressures leads to the IVC being stented open by high distending pressures
 - Diameter >2 cm, 84% sensitive,100% specific RAP > 8 mm Hg
 - Respiratory variation in mitral and tricuspid diastolic velocities

Clinical Caveats for the Diagnosis and Management of Tamponade

- Rapid accumulation of small amounts of fluid may lead to tamponade, severity is not merely a function of the volume of pericardial fluid
- Chambers may not collapse because of high pressures
- Tamponade post cardiac surgery is atypical

The etiology of pericardial tamponade (most common causes are pericarditis, iatrogenic pericardial fluid, malignancy, idiopathic, MI, ESRD, CHF, collagen vascular disease, TB, other infections, and trauma) and the drainage procedure (pericardiocentesis) are described in more details in Chapter 40.

Echocardiographic Approach to Pump Failure

• Large hypokinetic LV → LV systolic function → global or regional wall motion abnormalities → inotropy/IABP/cath lab

Echocardiographic approach to LV systolic function

LV systolic function assessed by measuring EF: EDV-ESV/EDV

• Normal > 55%, Mild > 45 < 54%, Moderate > 30 < 44%, Severe < 30%

Wall motion abnormalities:

- Global or regional
- Assess thickening and movement in coronary artery territories
- Qualify by using the segmental model

Echocardiographic approach to RV dysfunction

- RV function assessment mostly qualitative
- RV free wall motion is towards the apex
- Look for thickening of the RV free wall
- Look at tricuspid annular motion

RV dysfunction - asses the following

- Size of the RV-normally 2/3rds of the LV, when size of RV = LV moderate dysfunction, RV size > LV size severe dysfunction
- Movement of the RV free wall is diminished towards the apex
- Motion of the tricuspid annulus, normal > 1.8 cms
- Septal movement: barometer of relative pressure between the LV and RV. In the case of RV pressure overload, the septum moves towards to LV in systole, in RV volume overload septum

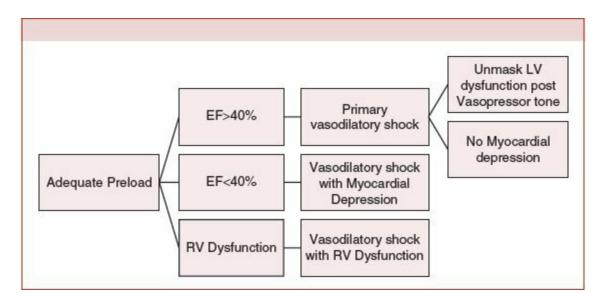
moves towards the LV in diastole.

Echocardiographic approach to hypovolemic shock

- Small hypercontractile LV
- Small LVEDA < 5.5 cms
- Assess volume responsiveness → aortic flow variation index = 100×/V peakmax-Vpeakmin)/(Vpeakmax + V peakmin)/2: >12% indicates volume responsiveness
- → Change in the diameter of IVC, DIVC = 100 × (IVCinsp-IVCexp)/IVCinsp: >18% indicated fluid responsiveness

Echocardiographic approach to septic shock

Figure 2. Echocardiographic Work-up of Septic Shock



Septic Shock:

- Establish adequate preload
- Use echocardiography to establish sepsis with normal EF; use echo post vasopressor administration to unmask LV dysfunction, and to identify sepsis with impaired EF or sepsis with RV dysfunction

Echocardiographic approach to tension pneumothorax

- Absence of lung sliding
- Doppler evidence of pulsus paradoxus and respiratory variation in transmitral flow

Echocardiographic approach to SAM (systolic anterior motion)

• Hypertrophic cardiomyopathy or severe flow acceleration through the LVOT \rightarrow Anterior mitral valve leaflet sucked into the LVOT \rightarrow SAM

ULTRASOUND-GUIDED PLACEMENT OF CENTRAL VENOUS CATHETERS (CVC)

- Variants of the typical anatomy are common.
- Arteries and veins are found in an atypical position 3%–10% of the time and their size maybe too small for cannulation (3%–5%). Therefore, the "landmark" technique is associated with a relatively high incidence of mechanical complications (pneumothorax, hemothorax, arterial cannulation, injury to the arteries and veins).
- Ultrasound (US) guidance can both expedite the placement of CVCs and reduce the related complications. However, operators must be trained in a standardized program and use standardized US imaging techniques and safety steps.

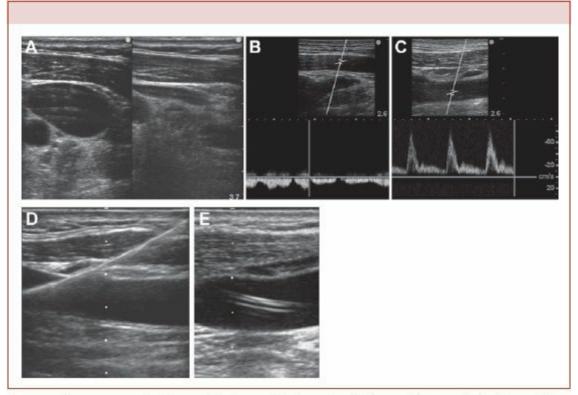
Procedural Standards for CVC Placement

- Pre-procedural checks:
 - Critically evaluate the need for CVC placement (risk vs. benefit assessment)
 - Obtain consent for the procedure
 - Check is patient's condition is appropriate for safe placement (stop heparin infusion, correct thrombocytopenia and coagulopathy (and other modifiable risk factors) if time and clinical condition allows)
 - Recruit team (assistance, supervising operator if needed, nurse), secure equipment
 - Perform safety check (including site verification) for the procedure
 - Follow institutional and national safety standards and maintain sterile precautions

Standardized Imaging Required Before and During the Placement of Internal Jugular and Femoral CVC (All Images are Archived)

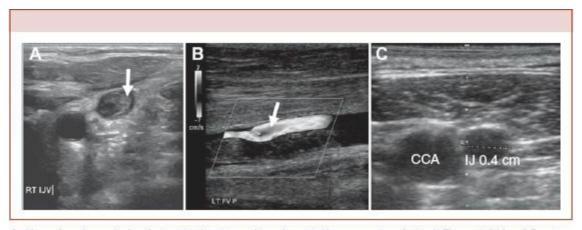
- Visualize target (internal jugular or femoral) veins and the adjacent arteries; document compressibility of the veins. This step allows to diagnose if the veins are too small for cannulation, are in an atypical anatomical location, or if they have thrombus in them (thrombus can be seen and will lead to the loss of compressibility). Obtain side-by-side pre- and post-compression images.
- Document appropriate velocity flow in both artery and vein using pulse-wave Doppler imaging. Color Doppler maybe used to visualize vessels but Doppler evaluation is mandatory to confirm appropriate flow.
- Visualize the needle as it is approaching the vein
- Visualize and confirm the presence of the guide-wire in the vein before dilating the vessel (note: a longitudinal view is superior to cross sectional view).
- Visualize and confirm the presence of the catheter in the vein once the placement is completed (again, longitudinal view is superior to cross sectional view).

Figure 3. Images of Standardized US Exam for US-Guided CVC Placement



A: pre and post-compression image of the internal jugular vein and the carotid artery (in dual image/sideby side mode); B: Doppler mode image of the internal jugular vein; C: Doppler mode image of the carotid artery; D: guide-wire visualized in the vein; E: catheter visualized in the vein.

Figure 4. Most Common Abnormal Findings During US Examination



A: thrombus (arrow) developing in the internal jugular vein (cross sectional view); B: partial blood flow is seen (arrow) around the thrombus; C: abnormally small internal jugular vein (CCA: common carotid artery; I]: internal jugular vein).

Standardized Training of Operators for US-Guided Placement of CVC

- Web-based, self-directed learning programs:
 - Prevention of CVC-related bloodstream infections, standardized sterile technique
 - The use of US imaging for the placement of CVC (instructional video and narrated slide show), followed by a multiple choice (pass/fail) test
- Simulation based practice and competency test (1 hr) at our simulation center (test based on the scores standardized in our study)
- Less-experienced operators (interns) are offered additional practice sessions in the simulator and in the vascular US laboratory
- Less-experienced operators are required to be supervised by experienced operators for their first 5

procedures (which have to be performed free of complications)

Steps for Enhancing the Safety of Subclavian Catheter Placement

• Subclavian veins should only be dilated and CVC be placed once it is confirmed that the access needle (or small gauge angio-catheter) is placed into the vein and not into the artery. This reduces the incidence of inadvertent arterial placement.

RADIOLOGIC IMAGING

YUKA OKAJIMA, MD • HIROTO HATABU, MD

ICU PORTABLE CHEST X-RAYS (CXR)

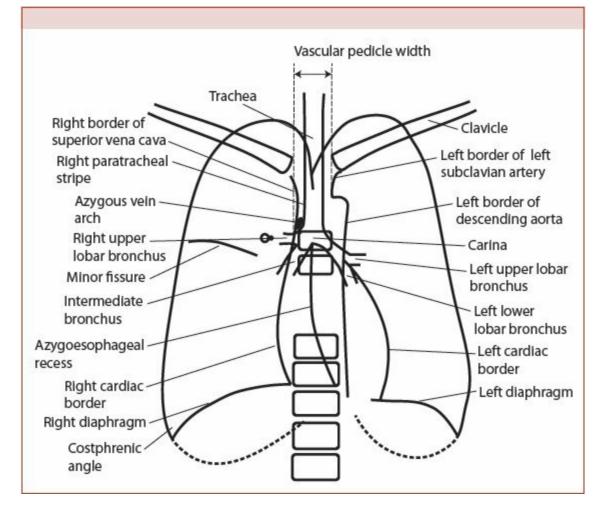
Recommended Indications

• Patients with acute cardiopulmonary disorders and receiving mechanical ventilation

Guide to Interpretation (Figure 1)

- Check patient's identity and the date of the study: make sure the subject is correct
- Evaluate the technical quality of the image
- Check the position of the supporting tubes and lines
- Check for abnormal air collections (pneumothorax, pneumomediastinum, pneumopericardium, or intraabdominal free air)
- Evaluate the cardiovascular status (the heart size and the width of the pulmonary vasculature) and the mediastinal width
- Note: The mediastinal lines are helpful to depict abnormal findings, although they are often obscured on portable CXR
- Check for abnormal pulmonary opacities and pleural effusions
- Check for bone or soft tissue abnormalities
- Compare with the prior studies

Figure 1. Image Components of Chest X-rays: Mediastinal Lines and Stripes



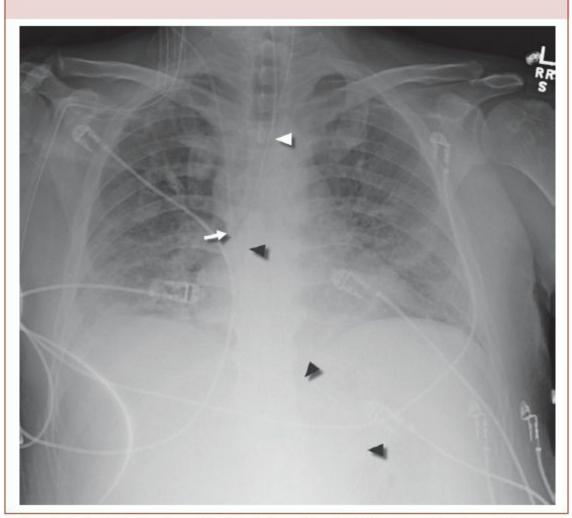
Characteristics of Portable CXR (Figure 2)

- The anterior—posterior (AP) supine position magnifies the mediastinal structures, compared to the posterior—anterior (PA) upright position
- \bullet Cardium: magnified up to 14%, upper mediastinum: magnified up to 50%
- The supine position may lead to vascular redistribution
- Low lung volumes due to poor inspiration may make the heart, the superior mediastinum, and the pulmonary vasculature appear prominent

Supporting Tubes and Lines Endotracheal Tube

- Check the position of the distal tip: rule out abnormal positioning
- Measure the distance from the distal tip from of the carina
 - Ideal position: 2 cm above the lower edge of the carina to just below the clavicle with the neck in the neutral position
 - Neck flexion and extension cause a 2 cm descent and ascent of the tube, respectively
 - The tip positioned at Th3–4 level is considered safe when the carina is invisible
 - Carina: at Th5–7 level, vocal code: at C5–6 level
- Check for complications: intratracheal or intraesophageal foreign materials (e.g., dislodged teeth), tracheal injury, subcutaneous emphysema, pneumomediastinum

Figure 2. Portable Chest X-ray: The Projection of Supporting Lines and Tubes



Endotracheal Tube Tip (White Arrow Head); Right Internal Jugular Catheter Tip (White Arrow); Nasogastric Tube (Black Arrow Heads)

Central Venous Catheter

- Check for procedure-related complications: pneumothorax, subcutaneous hematoma, and hemothorax
- Ideal position for the catheter tip: in the superior vena cava (SVC) about slightly above the right atrium (landmark: 1st intercostal portion)
 - Right and left brachiocephalic veins unite behind the first right costal cartilage
- Delayed complications: venous obstruction, vessel perforation
 - Radiographic findings indicating vessel perforation: mediastinal widening, enlargement of the cardiac silhouette, pleural effusions
 - Radiographic findings suggesting impending vessel perforation: curving of the catheter tip, direct placement of the catheter tip against the wall of the SVC

Nasogastric Tube

Check the proximal lateral hole (generally located within 10 cm proximal to the tip) located in the stomach

Chest Drainage Tube

- Check the position of the distal tip and side holes, and the way the tube runs
- Ideal position of the tip: apical for air, posteroinferior for fluid
- Check side holes in the thorax

- The tube generally runs outside lung fields in a gently curving course
- The tube running in a straight course may often be intralobar positioning
- Check for procedure-related complications: displacement (under the skin, intralobar, subdiaphragmatic, intraparenchymal), hemorrhage at insertion sites (e.g., intercostal arteriovenous injury), lung injury, diaphragmatic injury, intraabdominal organ injury

Swan-Ganz Catheter

- Ideal position of the tip: inside the right or left main pulmonary artery, no further than proximal interlobar pulmonary artery
- Check for complications: displacement, injury of pulmonary artery, pulmonary infarction

Intra-Aortic Counterpulsion Balloon (IABP) Catheter

• Ideal position of the distal marker: in the proximal descending aorta 2 cm below the aortic arch

CHEST CT

Indications for Contrast Enhanced CT (CECT)

- Evaluation of vascular diseases (aortic aneurysm, aortic dissection, pulmonary embolism, etc.) and mediastinum (see Figure 3 for cross-sectional anatomy)
- Check for active bleeding (trauma, hemothorax)
- Check for abscess, and empyema
- Note: In evaluation of active bleeding and aortic disease, pre-contrast CT is essential: hematoma is sometimes difficult to depict on CECT
- Evaluation of pulmonary parenchyma, usually does NOT require contrast media

Evaluation Before Contrast Injection

- General status: hemodynamic, neurologic status
- H/O significant allergies and asthma
 - Consider oral steroid premedication
- H/O renal diseases, diabetes mellitus, congestive heart failure, multiple myeloma
- Medications of concern: metformin, nephrotoxic drugs (NSAIDs, aminoglycosides, etc.)
 - Metformin should be held for 48 hrs after contrast media injection
 - Renal retention may lead to the retention of metformin, which may lead to lactic acidosis
- Other medications of concern: beta-blocker, calcium channel blocker, etc.
- Renal function: check serum BUN and creatinine, estimated GFR (eGFR)
- Cardiac function → consider reduction of contrast dose in patients with cardiac dysfunction

Classification of Severity and Manifestations of Adverse Reaction to Contrast Media

- Mild (self-limiting): nausea, vomiting, cough, headache, dizziness, itching, flushing, rash, facial swelling, nasal stuffiness, chills, sweats
- Moderate (frequently requiring prompt treatment): tachycardia, bradycardia, hypertension, erythema, dyspnea, bronchospasm, wheezing, mild hypotension
- Severe (often life-threatening, requiring aggressive treatment): laryngeal edema, profound hypotension, clinically manifest arrhythmias, convulsion, unresponsiveness, cardiopulmonary

arrest

• Delayed reaction: nausea, vomiting, headache, itching, skin reaction, fever, abdominal pain, diarrhea

Contrast-Induced Nephrotoxicity

- Dose-dependent (Frequency: intra-arterial injection > intra-venous injection)
- Serum creatinine level peaks within 2–5 d
- Usually transient; serum creatinine returns to the baseline within 14 d
- Risk factors for acute renal failure: pre-existing renal dysfunction (risk: eGFR < 30 ml/min: 7.8%, 30 < eGFR < 40 ml/min: 4.6%, eGFR > 40 ml/min: 0.6%), diabetes mellitus with renal dysfunction, congestive heart failure, dehydration, multiple myeloma, elderly (>70 y.o.), concurrent use of nephrotoxic drugs (e.g., NSAIDs, aminoglycosides), high-dose injection of contrast media, multiple injection within 72 hrs
- Note: The severity of contrast-induced nephrotoxicity greatly depends on the extent of pre-existing renal dysfunction
- Patients w/diabetes and chronic kidney disease have four-fold higher risk of acute renal failure than those w/o diabetes or preexisting renal dysfunction

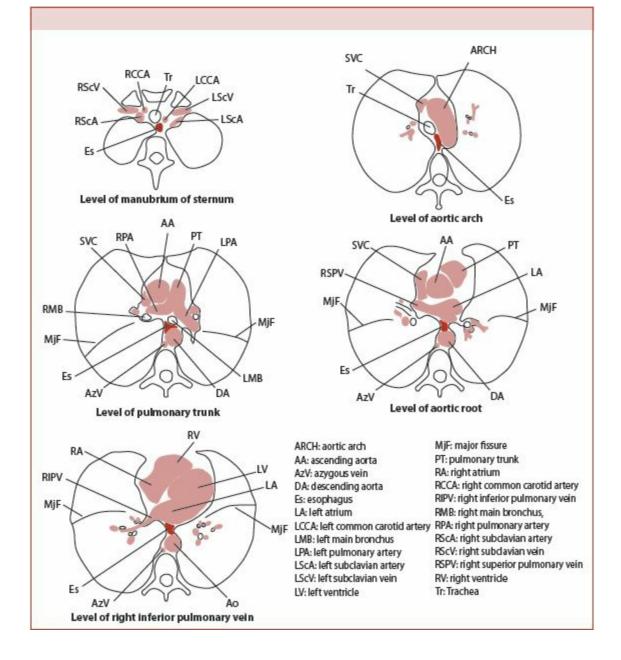
Recommendation for Prevention of Contrast-Induced Nephrotoxicity in Patients with Risk Factors

- Extracellular volume expansion may be most effective
- Recommended protocol of hydration (Br J Radiol. 2003;76:513)
 - For patients w/o contraindication to oral intake: oral intake of at least 500 ml of water (or soft drinks) before and 2,400 ml during the following 24 hr
 - For patients unable to intake orally w/o congestive heart failure: IV infusion of 0.9% saline at 100 ml/hr, beginning 4 hrs before the contrast media injection, continuing for 24 hr
- Stop concurrent use of nephrotoxic drugs and diuretics for at least 24 hr
- \bullet Consider reduction of dose if eGFR < 60 ml/min; consider alternative examinations if eGFR < 30 ml/min not under dialysis

Recommendation for Prevention of Contrast-Induced Anaphylaxis

- Prophylaxis is not completely protective, but reduces the incidence
- Indications: H/O respiratory adverse reaction to contrast media, H/O severe asthma, H/O significant allergies
- Note: With H/O severe adverse reaction, consider alternative examinations
- Recommended Protocol:
 - 32 mg methylprednisolone PO 12 and 2 hr before contrast injection (Eur Radiol. 2001;11:1720)
 - 50 mg prednisone PO 13 hrs, 7 hrs and 1 hr before contrast injection + 50 mg diphenhydramine IV/IM/PO 1 hr before contrast injection (*Catheterization and Cardiovascular Diagnosis*. 1995;34:99)
- Note: corticosteroids are not effective if given <6 hrs before contrast injection
- Use nonionic low-osmolality contrast media
- Consult your institution's guidelines

Figure 3. Cross-sectional Anatomy of the Thorax

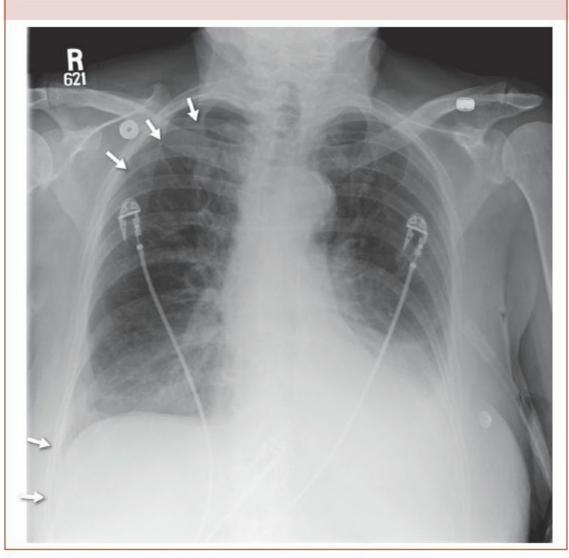


RADIOGRAPHIC FINDINGS IN THORACIC DISEASES

Pneumothorax (Figure 4)

- Check not only apices, but also basilar and lateral portion, esp. costophrenic sulci and cardiophrenic sulci
 - In the supine position, intrathoracic air extends from basilar ventral to superior ventral and lateral portion
- CXR: visualization of visceral pleural line, basilar hyperlucency, deep sulcus sign
- Mimickers: skin folds, lateral aspects of the scapula
- Note: Visceral pleural line is usually traced as a sharp thin line over the entire length
- Check for findings suggesting tension pneumothorax: lower deviation of the diaphragm, flattening of the cardiac border, deviation of the mediastinum to the opposite side
- Note: Tension pneumothorax in patients with stiff lungs may sometimes be difficult to depict because of no mediastinal shift

Figure 4. Right Pneumothorax and Bilateral Pleural Effusions



Right Pneumothorax is Marked by Upper Arrows Outlining the Lining of the Lung

Pne umome diastinum

- CXR: Streaky radiolucency in mediastitium, "continuous diaphragm" sign (air connecting both hemidiaphragmatic domes due to air posterior to the pericardium), "double bronchial wall" sign, "V sign of Naclerio" (mediastinal air extending laterally between mediastinal pleura and diaphragm), air in azygoesophageal recess, subcutaneous emphysema
- In children: radiolucency outlining the thymus

Pulmonary Edema

- Pathophysiology
 - Increased hydrostatic pressure: cardiogenic (most common), noncardiogenic (volume overload, renal failure)
 - Decreased colloid osmotic pressure: hypoproteinemia, rapid reexpansion of the lung
 - Increased capillary permeability: anaphylaxis, physical trauma aspiration, chemical inhalation, drug-induced injury, vessel occlusion

Hydrostatic Pulmonary Edema

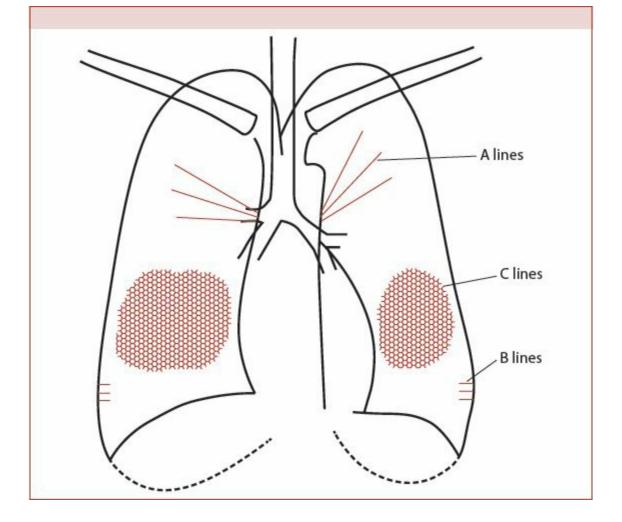
• Radiographic findings:

PCWP* (mmHg)	Type of Edema	CXR	ст
5-12		Normal	
12–17	Engorgement of pulmonary vessels	Pulmonary vascular redis- tribution (cephalization), enlarged azygous vein, widened vascular pedicle	Enlargement of pulmonary vessels
17–25	Interstitial edema	Perihilar haziness, vascular haziness, peribronchial cuffing, septal lines (Kerley lines), thickened fissures, pleural effusion	Smooth interlobular septal thickening, peribronchovas- cular thickening
>25	Alveolar flooding edema	Tiny nodular opacity, consolidation	Ground-glass opacities in a perihilar or dependent portion, centrilobular ground-glass nodules, consolidation

^{*}PCWP, pulmonary capillary wedge pressure

- Vascular pedicle (Figure 1): the distance between the point at which SVC crosses the right main bronchus and the point at which the left subclavian artery takes off
- Kerley lines (Figure 5):
 - A lines = long fine lines radiating from hilum in the upper lungs
 - B lines = short parallel lines perpendicular to pleura in peripheral lungs
 - C lines = "lace-like" polygonal lines or reticular linear opacities (least common)

Figure 5. Kerley Lines



• Note: RUL-predominant, asymmetric distribution may often be due to mitral regurgitation

Acute Lung Injury (ALI)/Acute Respiratory Distress Syndrome (ARDS)

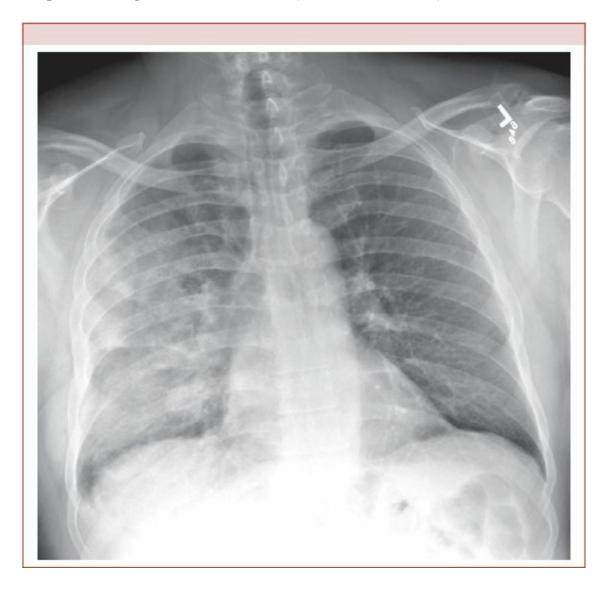
- The most severe permeability edema with diffuse alveolar damage
- Abnormal radiographic findings may appear later (12 hrs) than clinical onset of respiratory failure
- No cardiomegaly or pleural effusion
- CXR:
 - 1st (exudative) stage: perihilar patchy opacities throughout bilateral lungs, widespread bilateral massive consolidation, air bronchogram, gravitational gradient
 - 2nd (proliferative) stage: inhomogeneous consolidation and/or ground-glass opacities
 - 3rd (fibrotic) stage: reticular opacity, subpleural and intrapulmonary cysts
- CT: bilateral ground-glass opacities, bilateral homogeneous consolidation, traction bronchiectasis, interlobular septal thickening, intralobular reticulation
- Note: differential findings of ARDS from hydrostatic edema: peripheral distribution, absence of pleural effusion, slow resolution, intubated (ARDS tends to cause severe hypoxemia)

Pneumonia

- Radiographic findings are generally non-specific
- DDx: atelectasis, pulmonary hemorrhage, noninfectious lung inflammation, pulmonary edema, ARDS
- Radiographic patterns: (i) lobar pneumonia, (ii) bronchopneumonia, (iii) interstitial pneumonia
- Indications for CT: Suspected pneumonia w/o apparent abnormal findings on CXR, with subtle finding compared with severe symptoms, and w/ poor response for treatment

- Estimating pathogen is essentially difficult: some findings may strongly suggest a specific pathogen
- Lobar pneumonia (Figure 6): Streptococcus pneumoniae, Legionnaires' bacillus, Klebsiella pneumoniae
- Cavitation: *Staphylococcus aureus* (abscess), *Haemophilus influenzae*, *S. pneumoniae*, Fungal infections, Tuberculosis, Septic emboli

Figure 6. Legionella Pneumonia (Lobar Pneumonia) on AP Chest XR



Lobar Pneumonia (Alveolar Pneumonia)

- Disease progress: peripheral alveoli surrounding alveoli through Kohn holes and Lambert holes
- Lobar distribution, preserved or increased lung volume
- CXR: consolidation w/ surrounding lobular opacities, air bronchogram, w/o volume loss
- CT: sublobar consolidation w/ clear boundary, air bronchogram, bulging fissures

Bronchopneumonia (Lobular Pneumonia)

- Disease starts as bronchitis or bronchiolitis, extending to the surrounding alveoli
- Segmental and inhomogeneous distribution with volume loss due to mucus plug and/or narrowed airways
- CXR: inhomogeneous opacity, lobular opacities, peripheral atelectasis
- CT: small ill-defined centrilobular nodules, panlobular opacities, bronchovascular thickening, segmental opacities

• Pathogen: various bacteria (S. aureus, H. influenzae, Pseudomonas aeruginosa), mycoplasma

Pulmonary Tuberculosis (Secondary)

- Predominant location: apical and posterior segments of right upper lobes, apicoposterior segment of left upper lobe, and superior segment of bilateral lower lobes
- Segmental distribution
- Often: w/ cavitation; lymphadenopathy is rare
- CXR: consolidation, patchy opacities, nodular opacities
- CT: centrilobular nodules (dense, w/ clear boundary), centrilobular branching opacities, nodular opacities, acinar opacities (tree-in-bud pattern), bronchial/bronchiolar opacities, satellite lesions

Mycoplasma Pneumonia

- Wide-spreading opacities
- Segmental distribution, lower lobe predominant
- CXR: systematic peribronchovascular interstitial thickening, patchy opacities, segmental/lobular consolidation, reticular opacities, small pleural effusion, hilar adenopathy
- CT: peribronchial opacities (parahilar predominant), centrilobular nodules, ground-glass opacities, unilateral patchy inhomogeneous consolidation, reticular opacities, small pleural effusion (20%), hilar adenopathy

Respiratory Viral Pneumonia (e.g., influenza virus)

- CXR: normal or only hyperinflation (in early disease), diffuse small nodular opacities, indistinct peribronchovascular interstitial opacities, reticular opacities, septal lines, ground-glass opacities, patchy opacities
- CT:
 - Bilateral ground-glass opacities, consolidation, reticular opacities (crazy-paving appearance)
 - Bronchial wall thickening, centrilobular nodular opacities, air trapping

Systematic Viral Pneumonia (e.g., varicella-zoster virus)

- CXR: multiple bilateral nodules, ground-glass opacities
- CT: bilateral diffuse dense nodules with surrounding ground-glass opacities

Pneumocystis Pneumonia

- Perihilar and basilar predominant distribution
- Pleural effusion, hilar lymph adenopathy: rare
- CXR: normal in 20%–30%. Bilateral diffuse symmetric reticular and/or ground-glass opacities → consolidation, air bronchogram
- CT: bilateral patchy mosaic appearance, diffuse ground-glass opacities, linear/ reticular opacities, air-filled spaces, pneumothorax
- Findings suggestive of combined diseases to pneumocystis pneumonia:

CXR Appearance of Complex/Combined Pulmonary Diseases					
Findings	Suspected Combined Diseases				
Nodular opacities	 Infection: e.g., bacteria, mycobacteria, airway invasive aspergillosis, cytomegalovirus Exacerbation of underlying disease: malignant lymphoma, collagen vascular diseases, metastases 				
Pleural effusion or mediastinal/hilar lymph adenopathy	 Infection or other diseases: e.g., pulmonary tuberculosis 				
Cavitation/cyst formation	 Superimposed fungal/mycobacterial infection 				

• Note: With the prophylactic use of aerosolized pentamidine: upper lobe predominant, cystic disease, pneumothorax

Pleural Effusions (Figure 7)

- Small pleural effusions are difficult to depict on a supine CXR
- Lateral decubitus views are more sensitive, may detect >25 ml
- Detectable amount of effusions: upright lateral views >75 ml; upright PA views >175 ml
- CXR: [small-intermediate] obscured paravertebral area (esp. basilar area), obscured vascular marks around the diaphragm → [intermediate-large] obscured diaphragm, hypolucency of the ipsilateral lung field, thickened interlobar fissure, collapse of ipsilateral lung
- Findings suggestive of specific conditions:

Findings	Diseases/Conditions				
Rapid increase in pleural effusion	Hemothorax \rightarrow Indication for CT				
Loculated effusion, "Split pleural" sign (enhancement of both parietal and viscera pleural surfaces), extrapleural fat thickening >2 mm w/ increased density	Exudative effusion caused by infection, empyema malignant disease, abdominal inflammatory disease, collagen vascular disease				
Gas bubbles in pleural space	Empyema due to gas-producing bacteria bronchopleural fistula				
Unilateral effusion	Malignant disease, infection, congestive heart disease (right-sided), subdiaphragmatic disease, pulmonary embolism, trauma, chylothorax				

Figure 7. Congestive Heart Failure on AP Chest XR



Pulmonary Edema, Cardiomegaly and Bilateral Pleural Effusions are Seen

Hemothorax

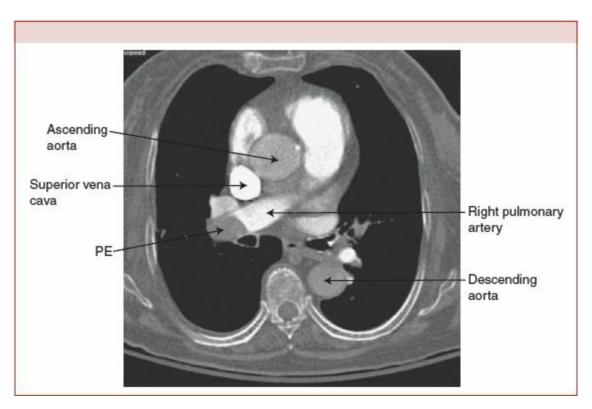
- Check the fluid density on non-contrast CT (fresh hematoma: 40–60 HU, simple fluid <20 HU).
- CECT may help to depict active bleeding and a bleeding point

Acute Pulmonary Embolism (PE)

- CXR: low sensitivity and specificity
- CT angiography/CT venography is recommended as the first imaging modality (sensitivity: 83%–100%, specificity: 89%–97%), Figure 8
- CT venography has the same sensitivity and specificity as ultrasonography for detecting venous thrombosis
- In patients with renal dysfunction, or severe iodine allergies: venous US is recommended after D-dimer testing; positive venous US results require treatment; pulmonary scintigraphy is recommended with negative US results
- In pregnant women and women in reproductive age: venous US is recommended after D-dimer testing; pulmonary scintigraphy may be the next imaging test of choice
- CXR: normal (most common); subsegmental atelectasis, pleural effusion, pleural opacities, elevated diaphragm, prominent pulmonary artery, decreased vascularity
- Suggestive findings of PE: Westermark sign (reduced vascularity distal to a large embolus; "knuckle sign" (steep distal tapering of an occluded vessel); Hampton hump (a pleura-based, wedge-shaped consolidation with convex border, representing pulmonary infarction)
- CECT: Check imaging quality; optimal contrast opacification is indispensable!
- Diagnostic CT findings for PE: Complete filling defect; partial filling defect surrounded by a rim of

- contrast media ("railway track" sign); enlarged less-enhanced artery (occluded artery), compared to adjacent patent arteries; peripheral filling defect
- Other findings: linear atelectasis (100%), pleural effusion (87%), consolidation, ground-glass opacity, Hampton's hump, dilated central pulmonary artery
- Check points:
 - "Saddle embolus" (embolus crossing the bifurcation and involving both main pulmonary arteries) in decompensating patients → consider a more aggressive intervention
 - Right heart strain (RV enlargement (RV/LV ratio ≥1), leftward bowing of the interventricular septum, reflux of contrast media into the IVC and hepatic veins) → associated with poor clinical course

Figure 8. Pulmonary Embolism (PE) in Right Pulmonary Artery



Aortic Dissection

- Classifications: see Figures in Chapter 30
- Stanford Classification (related to treatment recommendations)
 - Type A: all dissections involving the ascending aorta regardless of the site of origin
 - Type B: all dissections not involving the ascending aorta
- CXR: normal in 25%; irregular or obscured outline of aorta, different in size between ascending and descending aorta, LV dilatation, left pleural effusion, medial lower lobe atelectasis, widened upper mediastinum
- With calcified atherosclerotic plaque: displacement of calcified plaque from aortic outline
- CECT: high sensitivity and specificity (>87%)
 - Crescentic hyperdense hematoma within false lumen, intimal flap separating 2 aortic lumens, intimal calcification displaced from aortic wall

Thoracic Aortic Aneurysm

• Aneurysm: >50% increase in diameter compared to the expected normal diameter

- Normal average diameter of thoracic aorta: aortic root: 3.6 cm, ascending aorta: 3.0 cm, middescending aorta: 2.5 cm
- Location: arch > descending aorta
- Surgical indication: symptomatic patients, asymptomatic patients with the ascending aorta of $\geq 5-6$ cm, the descending aorta of $\geq 6-7$ cm, or with a growth rate ≥ 1.0 cm/y
- CXR: wide tortuous aorta, mediastinal mass adjacent to aorta
- CT: wide tortuous aorta, circumferential mural thrombus
- Ruptured aneurysm: extravasation of contrast media, hyperdense fluid collection or hematoma in the mediastinum, pericardium, pleural sac, or extrapleural space
- Note: "Crescent sign" (peripheral hyperdense crescent hematoma in aneurysm) indicates impending rupture!

Traumatic Rupture of the Thoracic Aorta

• Location: aortic isthmus (most common) > ascending aorta > descending aorta (least common)

Brain CT

Indication for Brain CT in Trauma Patients

- Loss of consciousness (more than transient)
- Altered mental status during observation
- Focal neurologic signs
- Clinically suspected basilar fracture
- Depressed skull fracture
- Penetrating wound (e.g., bullet)
- Suspected acute subarachnoid hemorrhage, intracranial hematoma

Check Points in Emergency Brain CT

- Check patient's identity and the examination date: make sure the subject is correct
- Check for emergency requiring immediate intervention: brain herniation (see next paragraph), mass effect (midline shift, narrowed ventricles, loss or obscuration of cisterns and fissures)
- Symmetricity
- Localized or diffuse abnormal lesion
- Hemorrhage (high density in acute phase, gradual decrease in density later), edema (low density)
- Trace brain surface; check for cisterns and fissures
- Size of ventricles
- In trauma patients: fracture, subcutaneous hematoma, foreign bodies (air, bone fragments, bullet); carefully evaluate the affected site and the opposite site (contre-coup injury)
- Note: make sure the very top and bottom slices are included!

Brain Herniation

Transtentorial Herniation

- Descending toward the posterior fossa
 - CT: widening of ipsilateral ambient and/or prepontine cistern, widening of contralateral temporal horn, disruption of suprasellar cistern, displacement of uncus into suprasellar cistern (anterior herniation), parahippocampal gyrus herniation (posterior herniation), entire hippocampal herniation (total herniation)

- Ascending displacement of cerebellum through tentorial incisura
 - CT: compressed midbrain bilaterally on posterolateral aspect ("spinning top" appearance), narrowed ambient cistern and/or quadrigeminal cistern

Hyperacute Cerebral Infarction (<12 hrs)

- CT: normal in 10%–60%.
- Subtle hypodense gray matter, obscuration or loss of gray—white matter separation, hyperdense intraluminal thrombus within cerebral artery (e.g., "hyperdense MCA sign"), narrowed ipsilateral sulci and/or sylvian fissure

Acute Cerebral Infarction (12 hrs-1 wk)

• CT: low density area (become more prominent than hyper acute phase), loss of gray-white matter separation, mass effect due to large infarction, hemorrhagic infarction after 2 days

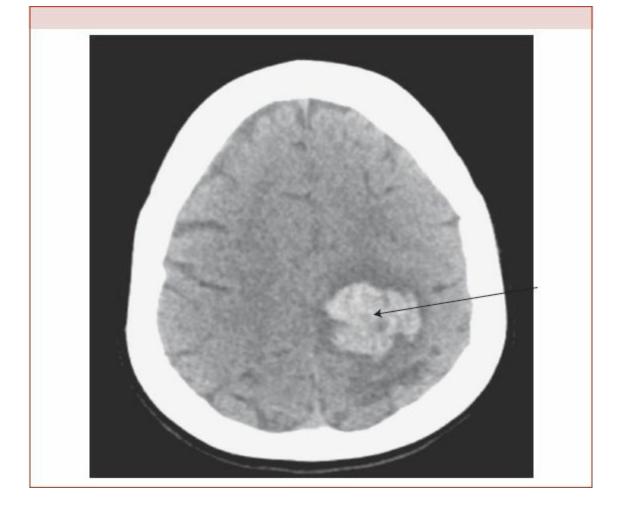
Intracerebral Hemorrhage *Hematoma (Figure 9)*

- CT:
 - Hyperacute (4–6 hrs): well-defined homogenous hyperdense lesion (continual for 1 wk) surrounded by low attenuation → early subacute (3–7 d): enlargened → late subacute (>1 wk): gradual decrease in density (resorption starts from peripherary toward the center) → chronic (>1 mo): isodense lesion surrounded by hypodense area

Cortical Contusion

- CT: sensitive to acute hemorrhage
- Poorly defined densities, "salt and pepper lesion" (mixture of high and low density = punctate hemorrhage and edema), diffuse cerebral swelling

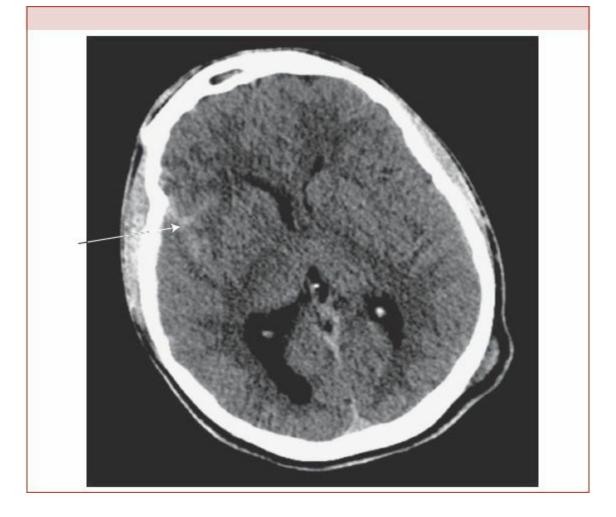
Figure 9. Intracerebral Hematoma



Subarachnoid Hemorrhage (Figure 10)

- CT: accuracy of depiction depending on amount of hemorrhage and timing of scan (highly accurate within 4–5 d from onset)
 - Increased density in cisterns and/or fissures, intraventricular hematoma due to reflux
- Complications: hydroencephalus (acute, delayed), cerebral infarction due to vasospasm, transtentorial herniation

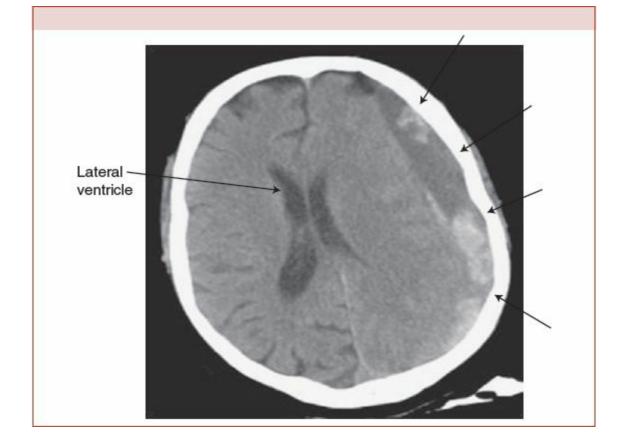
Figure 10. Subarachnoid Hemorrhage



Subdural Hematoma (Figure 1)

- Small subdural hematomas are easily missed (up to 40% of the time)
- CT: Extraaxial fluid collection, concave inner border, high (<1 wk) ~ low (>3-4 wk) density, "swirl" sign (mixture of hyperdense fresh bleeding and hypodense old clot = active bleeding)
- Check for the extent of mass effect (loss or obscuration of adjacent sulci, ipsilateral ventricular compression, inward displacement of corticomedullary junction, midline shift
- Caution needed for bilateral hematoma (often w/o midline shift): too small ventricles for the age

Figure 11. Subdural Hematoma with Midline Shift



Epidural Hematoma

- Often associated with skull fracture
- CT: Extra-axial biconvex homogenous fluid collection, mass effect, marked stretching of vessels
- Differentiation from subdural hematoma: usually not cross suture lines, convex inner border, homogenous ("swirl" sign is rare)

Herpes Simplex Encephalitis

- CT: Usually normal in first 3 d
- Ill-defined low attenuation in bilateral temporal lobes (medial predominant) and insulae, narrowed sylvian fissure and lateral ventricle, hemorrhage
- Putamen is usually spared with well-defined border

NURSING STANDARDS IN CRITICAL CARE

MARY PENNINGTON, RN, MS

Connect with and know your patient as an individual person, humanize a highly technological environment and ensure a safe passage for patients and families.

CRITICAL CARE NURSING WORK FLOW

Shift Report

- Prepare for hand-off/shift report
 - Review medical record, flow sheet, medication administration record, labs, and physician orders
 - Evidence suggests shift report is optimized when done at the bedside in the presence of the patient
 - Enhances patient safety by promoting nurse-patient and nurse-nurse communication
 - Increases the patient's and family's trust and sense of security
- Receiving hand-off/shift report
- Organize your report sheet the same way every day (see sample report sheet)
 - Review the nursing and medical plan for the shift
 - Ventilator weaning
 - Medication weaning
 - Activity/mobilization
 - Psychosocial and emotional needs
 - Family needs
- Preliminary assessment is done as part of the shift hand-off
 - Includes patients level of consciousness (LOC); airway, breathing, circulation (ABCs), tubes, lines and drains; wound dressings; medication dosage and rates of intravenous (IV) infusions; amount of fluid left in the IV infusion bags; invasive line leveling, safety issues
 - Document the first set of vital signs, ventilator information, infusion rates, pain/ agitation and note that you have re-leveled to the phlebostatic axis and zeroed the transducers
 - Print an ECG rhythm strip and a copy (if an electronic copy is not automatically saved) of all transduced pressures from the physiologic monitors

Strategize Your Shift

- Organize the sequence of activities
 - Prioritize and cluster activities to provide periods of rest for the patient
 - Traveling to a procedure/test
 - Dressing changes/bed bath/oral care/turns/back care/repositioning
 - Intravenous catheter (commonly called "line") changes/tubing changes
- Knowing the time the family plans to visit will help you to create opportunities for quality family visits
- Mobilizing the patient: plan getting out of bed and the physical therapy sessions, coordinate them with family visits

Assessment

The nurse continuously assesses and monitors physiological data, interpreting it based on the patient's physical, emotional and psychological state and response. The work-flow changes minute to minute driven by these assessments.

- Airway:
 - Is the patient's airway secure?
 - If intubated: check for secure and stable endotracheal tube (ETT) and record position
 - Ability to maintain open airway is related to decreased level of consciousness and muscular skeletal ability
 - Need for suction?
 - Does the patient need to be intubated due to lack of airway protection, respiratory decompensation or other reasons?
- Breathing:
 - Rate: <25/min (expected as upper limit of normal)
 - Quality, depth, pattern
 - Equal and symmetrical chest excursion, bilateral breath sounds?
 - Able to complete a sentence?
 - If on mechanical ventilation is the patient comfortable and synchronous
- Assess Circulation:
 - Level of consciousness
 - Heart rate
 - Rhythm
 - History of cardiac dysrhythmias?
 - Evaluate a rhythm strip: rate, presence/configuration of P waves, length of PR interval, length of QRS complex, presence and configuration of T waves, length of QT interval, presence of extra waves (u waves) and presence of dysrhythmias
 - Central and peripheral pulses
 - Skin color and temperature
 - Continuous infusions (commonly called "drips")?
- Tubes, lines and drains
 - Chest tubes patent and secured: drainage, suction, air leak
 - Trace patient IV tubing from patient back to the pumps
 - Assure that they are patent, secure, and labeled
 - LOOK at your drips: check if they are the correct medications as ordered, correct route and dose: ALWAYS DOUBLE CHECK
 - Adequate IV volume left
- Know the code status of your patient
- DOCUMENT assessment on the ICU flow sheet (whether paper or electronic format depending on the institution you work at) in real time
- Environmental Assessment/Checks
 - Check arrhythmia alarms are they on and appropriately set to alarm
 - Suction/Ambu set-up
 - Emergency drugs available in room (based on patient diagnosis)
 - Identify and label IV access catheter as your "emergency IV push line"
 - Know where the emergency equipment is located

- Identify hemodynamic, respiratory, sedation and pain parameters being treated and titrated
- Infusates (commonly called "Drips")
 - Check label to make sure that what is running correlates with what is programmed in IV pump and what was ordered
 - Label tubing identifying which drug is hanging where
 - Check infusion rate
 - Check all IV connections making sure that tubing is luer locked and infusing correctly
 - Check volume left and if volume in bag or syringe is low, make sure that another infusion bag is immediately available

Planning Care

- This time perform a complete assessment (see Appendix II). Compare and contrast your findings to previous 24 hrs
- Address present and potential problems:
 - Pain and sedation, altered hemodynamic states, impaired physical mobility, impaired skin integrity, deficient fluid volume, nutrition, sleep deprivation, patient/family coping
- Evaluate fluid status of patient and impact on other body systems. Assess electrolytes and identify cause of electrolyte imbalance, clinical manifestations, treatment
- Evaluate patient progress and possible need for revisions in plan of care
- Prepare for interdisciplinary rounds
- Seek consultation from knowledgeable colleagues: nurses, physicians, respiratory therapists, pharmacists, social workers, chaplains
- Access resources to assist with clinical dilemmas and problem solving
- Prioritize and sequence activities for the patient by clustering some, and providing periods of rest. Activities: dressings, turns, line changes, traveling for a test, getting the patient out of bed to a chair or ambulating. Consider when the family is coming and create opportunities for a quality visit for all.
- Be Flexible! Your plan for the day is highly subject to change based on the patient's condition.
- Complete your note before you give report which will help identify salient issues
- Give hand-off report

Ensure the Accuracy of Technology and Physiological Data

- Priming of the Pressure Tubing:
 - Air bubbles in the tubing system are a frequent and important cause of error in hemodynamic monitoring creating a dampened waveform (even tiny air bubbles)
 - Air-free priming
 - Remove all air from the flush solution
 - Entire tubing system should be flushed
 - Stopcocks, luer-lock interconnections, and transducer common locations of air entrapment
- Leveling of the Transducer
 - Level transducer to the phlebostatic axis of the patient
 - Intersection of the 4th ICS and ½ the anterior-posterior diameter of the chest
- Rationale:
 - Eliminates effects of hydrostatic forces on hemodynamic pressures
 - Ensure the transducer is leveled before zeroing and/or obtaining pressure readings

- Note: re-level the transducer with any change in the patient's position to assure accurate readings
- Zero Referencing:
 - Rationale: ensure that pressures being measured reflect the patient's hemodynamics and not the effects of atmosphere or fluid in the system
 - Procedure:
 - Turn the stopcock port nearest the transducer off to the patient
 - Remove the dead end cap, opening to air
 - Activate the zero function key on monitoring device
 - Confirm that the monitor reads ZERO
 - Replace cap, turn stopcock open to patient, and confirm waveform on monitor
- Dynamic Response Testing/Square Wave Test:
 - Helps evaluate whether your monitoring system's dynamic response is accurate
 - Perform at the beginning of your shift and anytime you suspect values are not accurate
 - Done by activating the fast flush device on the transducer for 1–2 sec. Evaluate the 'bounce back'
 - You should see the waveform should square off oscillate (bounce) once and come back to rest

Nursing Preparation for Intra-Hospital Transport of Critically III Patients (also see Chapter 48)

The transport of critically ill patients to procedures or tests outside the ICU is potentially hazardous, and occurs only when urgently required for the provision of care. It is strongly recommended that a minimum of two people accompany a critically ill patient

- Pre-transport coordination and plan
 - Clarify urgency and rationale for test and procedure
 - How long will you be travelling?
 - How unstable is your patient?
 - What resources are available at the destination?
- What physician orders do you need? (Example: analgesia or sedation orders)
- If patient is now NPO and has an insulin drip, check blood sugar for hypoglycemia
- NPO appropriate amount of time
- Identify IV push line
- Are you going to need peripheral access?
- If going to MRI remove all metal, including electrodes
- Make sure the consents are all obtained
- Pre procedure preparation completed?
- Medications administered
- Pre-medications ordered and administered
- All critically ill patients need secure intravenous access and a secure airway before transport. A patient should not be transported before airway stabilization if it is judged likely that airway intervention will be needed
- Transport Equipment
 - A blood pressure monitor (or standard blood pressure cuff), pulse oximeter, and cardiac monitor/defibrillator accompany every patient
 - Resuscitation medications and equipment that may be necessary (not for every patient):
 - Defibrillator
 - Resuscitation drugs: epinephrine and anti-arrhythmic agents
 - Supplemental medications such as sedatives and narcotic analgesics based on patient needs
 - Intravenous fluids and continuous drip medication
 - All battery-operated equipment is fully charged and capable of functioning for the duration of the transport
 - ICU flow sheet
 - Suction for chest tubes (CT's) if required?
 - Oxygen tank/ambu and face mask
 - IV pumps
 - Elevator key to facilitate travel
- Accompanying personnel
 - Respiratory therapist if the patient is mechanically ventilated
 - Orderly to assist with transportation
 - If patient is hemodynamically unstable, a physician with expertise in airway management, advanced cardiac life support and critical care training should accompany the patient
 - If the patient is stable and a physician will not be accompanying the patient, orders or protocols are needed to permit the administration of medications and fluids by RN if needed
 - Nurse to provide continuity of care, monitoring of physiological data, and ensure patient safety

- Bag-valve ventilation is the most common method of mechanically ventilating patients during intrahospital transports. Portable mechanical ventilators are available and more reliably administer prescribed minute ventilation and desired oxygen concentrations. Some of our hospitals preferentially transport mechanically ventilated critically ill patients with transport ventilators. Make ventilation equipment available at receiving location.
 - Prior to transport, ETT position should be noted and secured and adequacy of oxygenation and ventilation is reconfirmed.
- Monitoring and documentation required:
 - Assure the same level of basic physiologic monitoring during transport as in the ICU.
- If the procedure will be long and the receiving unit is staffed by appropriately trained nurses, patient care may be transferred to those nurses. If care is not transferred, the ICU nurse remains with the patient until returned to the intensive care unit

Sleep Deprivation in the ICU Patient

Sleep duration and quality is now recognized as critical in the prevention and treatment of cardiovascular, lung and blood disease (National Heart, Lung and Blood Institute. 2007)

- Characteristics of sleep in the ICU
 - Fragmented
 - Short naps distributed over 24 hrs
 - Average uninterrupted sleep in ICU is 50 min to 2 hrs
- Increased arousals and awakening
 - BP measurements, temperature, suctioning, mouth care back care, turning, baths
- Factors associated with sleep disturbances in ICU patients
 - Environment noise, alarms
 - Clinical care
 - Mechanical ventilation
 - Sleep versus sedation
 - Staff conversations are one of the most disruptive noises
- Noise reduction strategies
 - Closing doors
 - Earplugs
 - Plan uninterrupted blocks of time with dimmed lights and decreased sound
 - Relaxation music
 - Increase staff awareness of noise, conversations in close proximity to patient
 - Maximize environmental opportunities to decrease noise
- Natural sleep versus sedation: assessment
 - Sedation does not imply quality sleep
 - Natural sleep
 - Spontaneous
 - Reversible with external stimuli
 - Circadian
- Interventions for sleep
 - Back massage improves quality and length of sleep
 - Clustering/timing clinical care activities to provide blocks of uninterrupted sleep
 - Collaboration with all providers to cluster care (x-rays, medications, procedures)

- Consider workflow in relation to clinical goal and patient impact: example ritual clinical habits such as bathing at 4 am.
- Mechanical ventilator sleep promotion strategies
 - Promote ventilator synchrony rest from weaning
 - Comfort pain/anxiety relief and thirst relief
 - Promote feeling of safety

Wound Care and Pressure Ulcers

National Pressure Ulcer Advisory Panel (NPUAP, 2007) Definition: localized injury to the skin and/or underlying tissue usually over a bony prominence, as a result of pressure, or pressure in combination with shear and/or friction

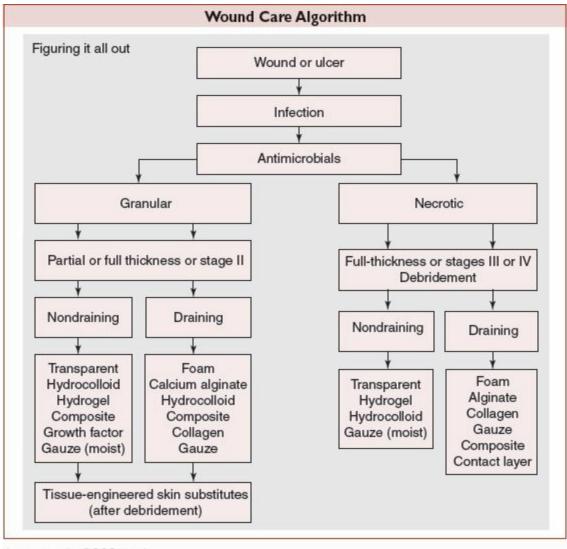
ICU patients are often immobilized and on bedrest due to hemodynamic instability, putting them at reat risk for skin breakdown and delayed wound healing

- Causes of Pressure Ulcers:
 - *Pressure:* perpendicular force results in compression of tissues between a bony prominence and an outside surface
 - Capillary pressure >32 mm will cause occlusion
 - Sustained disruption of blood flow S ischemia, hypoxia, tissue acidosis, edema, and eventually necrosis
 - Moisture: excess moisture directly affects the friction coefficient of skin: causing maceration
 - Immobility: oxygen deprivation to the affected area
 - Poor nutrition: wasting and excessive loss of lean body mass, dehydration
- Vulnerable pressure points in the bedbound body:
 - Most common pressure points sacrum and heels
 - Any bony prominence that experiences pressure: occiput, ears, scapula, elbows, spine, coccyx, iliac crest, lateral and medial knees, anywhere the leg touches the bed
- PREVENTION IS BEST PRACTICE: prevention strategies:
 - Assess skin on admission and daily using the braden scale. Check all bony prominences.
 - Daily Skin Care:
 - Mild cleansing agent for bathing; avoid hot water and *rubbing*. *Don't rub the red*. Apply lotion after bathing
 - Bowel and bladder program
 - Uncontrolled incontinence: cleanse, topical barrier. Absorbent underpads. Collection device
 - Use moisturizers for dry skin
 - Manage Incontinence:
 - Use absorbent cloth incontinence pads
 - Scheduled toileting: offer bedpan/urinal before each turn
 - Avoid diapers
 - Manage Nutrition
 - Nutrition screen on admission
 - Consult dietitian
 - Offer supplements, fluids
 - Assist patient with food choices
 - Consider calorie count
 - Manage friction and shear

- Repositioning:
 - Ceiling lift (ensure there are no folds in the sling if it is left under the patient)
 - Trapeze
 - Lift sheet
- Protect elbows/heels, areas exposed to friction with: transparent film dressings (Tegaderm®), skin protective barrier film, or protective dressings such as hydrocolloids (extra-thin Duoderm®)
 - Offload at-risk heels with pressure off-loading device (pressure-relieving heel protectors), vertically placed pillow with heels off mattress
- Mobilize patient; consider PT consult
- Pressure Ulcer Treatment
 - Basic Wound Care Principles:
 - If it's wet, wick it . . . If it's dry, moisten it . . . If it's necrotic, debride it . . . If it's infected, treat with anti-microbials
 - Cleansing
 - Debridement
 - Pressure Redistribution

Figure 1. The Braden Scale for Predicting Pressure Sore Risk

	BRADEN S	CALE FOR PREDICTII	NG PRESSURE SORE	RISK	
Patient's Name		Evaluator's Name		Date of Assessment	
SENSORY PERCEPTION ability to respond meaning- tully to pressure-related discomfort	Completely United Unresponsive (does not moan, flinch, or grasp) to painful stimuli, due to diminished level of con-eclousness or seds ton. Fig. 1 Imited ability to feel pain over most or body.	2. Very Limited Responds only to painful stimuli, Cannot communicate discomfort except by moaning or restlessorpes has a sensory impairment which limits the ability to feel pain or discomfort over 1/2 of body.	S. Sightty Limited Resports to verbal commands, but cannot always communicate disconfort or the need to be turned. Resports to the turned to the turned. Resports to the turned turne	No impairment Responds to verbal commands. Has no sensory deficit which would limit ability to feel or voice pain or discomfort.	
MOISTURE degree to which skin is exposed to moisture	Constantly Moist Skin is kept moistalmost constantly by perspiration, urine, etc. Dampness is detected every time patient is moved or turned.	Very Moist Skin is often, but not always moist. Unen must be changed at least once a shift.	Occasionally Moist: Skin is occasionally moist, requiring an extra linen change approximately once a day.	Rarety Moist Skin is usually dry, linen only requires changing at routine intervals	
ACTIVITY degree of physical activity	Bedfast Confined to bed.	Chairfast Ability to walk severely limited or non-existent. Cannot bear own weight and/or must be assisted into chair or wheelchair.	Walks Occasionally Walks occasionally during day, but for very short distances, with or without assistance. Spends majority of each shift in bed or chair	Walks Frequently Walks outside room at least twice a day and inside room at least once every two hours during waking hours	
MOBILITY ability to change and control body position	Completely Immobile Doss not make even stight changes in body or extremity position without assistance	Very Limited Makes occasional slight changes in body or extremity position but unable to make frequent of significant changes independently.	Slightty Limited Makes frequent though sight changes in body or extremity position independently.	No Limitation Makes major and frequent changes in position without assistance.	
NUTRITION <u>usual</u> food Intake pattern	1. Very Poor Neare eats complete meal. Rainely eats more than 1/2 or any bod of liter do fail 2 servings or less of protein (meet or dairy products) per day. Takes thuids poorly, Does not take alt huid detary supplement OR In NPO andor maintained on clear liquids or N°s for more than 5 days.	2. Probably inadequate Rarely eats a complete meal and generally eats only about 1/2 of any tood offered, Protein hake includes only 3 servings of meat or daily products per day. Cocastinatly will take a dietary supplement. OR receives less then optimum emount of liquid det or tube feeding	A. Adequate Eats over half of most meats. Eats a ball of 4 servings of protein (meat, daty products per day, Cocasionally will refuse a mest, but Usually take a supplement when officed OR is on a tube leading or TPN regimen which probatly meets most of nutritional needs	Excellent Eats most of every meal. Never retuses a meal. Usually eats a bial of 4 or more servings of meet and daily products. Occasionally eats between meals. Does not require supplementation.	
FRICTION & SHEAR	Problem Requires moderate to maximum sassistance in moving. Complete ifting without sliding against sheets it myosatile. Requently slides down in bed or chair, requiring frequent repositioning with maximum assistance. Spasibility, contractures or agitation leads to almost constent tictorion.	Potential Problem Mores feebly or requires minimum assistance. During a move skin probably sides to some extent against sheeke, chat, restraints or other devices. Maintains relatively good position in chair or be and of the time but occasionally slides down.	No Apparent Problem Moves in bed and in chalf independently and has sufficient muscle strength to lift up completely during move. Mainfains good position in bed or chair.		



(www.nursing2008.com)

- Moist Wound Therapy Dressings
- Nutrition
- Control of Infection

Transitioning to Intermediate Care and the Transfer Process

- Evaluate patient stability:
- Clarify that IV infusions are either discontinued or at an acceptable dose for intermediate care
- Remove all monitoring catheters (PA and arterial catheters) that are no longer needed
- Patient bathed, dressings changed, drainage bags emptied prior to transfer
- Ensure that all labs are done, results recorded and abnormal results treated and communicated to receiving nurse
- Transfer note either on Clinical pathway or nursing progress note completed
- Update all paperwork, all pending orders are taken off prior to transfer
- Call report, gather patient belongings and all appropriate equipment (respiratory equipment, pneumatic boots, IV pumps, medication...) to send with patient
- If patient requires telemetry to travel it is strongly recommended that the nurse accompany patient to intermediate floor

Figure 2. Sample Patient Report (Hand-off) Sheet

	Fig	gure 2. Sample Patien	t Report (Hand-of	ff) Sheet					
Room #:									
DOA:	DOB:	Precautions:		Code:					
DIAGNOS	IS:		NEURO: Neuro Checks q_hr GCS: Pupils: LOC: Neuro Checks q_hr Posturing: Posturing: ICP: Responsiveness?						
PMH/PSH: ALLERGIES:			CARDIAC? Rhythm: Rate: BP: CVP: PP/CSM:						
TESTS/PRO	OCEDUR	ES:	PULMONARY O ₂ Sat:	PULMONARY: VENTILATOR:					
Time:	Test/Proce	dure	RR: Labored? Airway: ET tube: Wean??	Rate: FiO ₂ : V _T : PS: Peep:	Rate: FiO ₂ : V _T : V PS:				
Pain: PCA/E: Settings: Diet:			GI: Ostomy: Stoma: LBM:						
TPN/Tube Ambulation			197730.25						
MEDICATI	ONS:		GU: Color/Amt:						
Name	D	osage							
LAB VALU	ES:		SKIN:						
+	Ca Se Ck Ck	CMB: oponin:	Color: Temp: Edema:						
Magnesium: Ionized Ca: Calcium:	pH pC pC	O ₂ : pCO ₂ :	IV Access: IVF: A-line: PA-line:						
Lactate: Albumin: Bilirubin: Phosphorus: PT			JP Drain(s) Output: Location:	Chest To Output: Air leak:		Drain(s) Type: Output:			
Courtesy o	f is Erica	Lopes Cabral RN,							

Head

- LOC, orientation, memory, language, emotional state, general appearance
- Pupils size, reaction, eye movements
- Hearing
- Vision
- Extremity strength
- ROM
- Gait (if applicable)
- LEVEL OF SEDATION
- Pain/character/location/intensity
- Oral assessment dentures? thrush?

Heart

- Point of maximal intensity (PMI) (L. midclavicular line at the 5th ICS)
- Rate/rhythm document strip/intervals, check alarm limits on
 - 12 lead EKG if needed?, check QT
- Heart sounds
- Edema
- Capillary refill/clubbing
- Peripheral pulses
- Extremity temperature
- Blood pressure (on admission both arms)
- CVP, PA pressures, PCWP, CO (if applicable)

Lungs

- Evaluate for patent airway
- Evidence of inadequate airway stridor, noisy respirations, supraventricular and intercostals retractions, flaring of nares, labored breathing with use of accessory muscles
- Respiratory rate/depth/pattern
- Auscultate breath sounds
 - Absent breath sounds, diminished breath sounds, crackles (rales), rhonchi, wheezes, pleural friction rub
- Cough, character of sputum
- Oxygen saturation
- Assess arterial blood gases (ABG's)
- Oxygen delivery
 - Nasal Prongs, Face mask, tracheostomy tube, endotracheal tube
- Assess ETT
 - Security of tube
 - Size
 - Position of tube (centimeter mark at lip line or nares)
 - No audible leak
- Tracheostomy size and confirm that there is a spare one in room
- Suction set up
- Chest tubes how much suction, mark drainage, check for air leak

- Palpate the neck and anterior chest for subcutaneous emphysema
- Chest x-ray results

Ventilator Assessment

- Equipment check: manual resuscitation bag, oxygen reservoir, tubing, and flow meter are at bedside (PEEP valve if >5 cm PEEP in use)
- Assess the ventilator tubing as follows:
 - Trace the tubing from the ETT to the ventilator, making sure all connections are secure
 - Empty water into the in-line water trap
 - Make sure the inspired air temperature is 31–37 °C
- Identify the mode of ventilation
- Check and confirm the ventilator settings
- Check the set PEEP level
- Note the peak inspiratory pressure (commonly referred to as PIPs)
- Note the minute ventilation
- Check essential ventilator alarms to ensure limits are set appropriately

Abdomen

- Pain/tenderness/distension
- Nausea/vomiting
- Nasogastric tube (NGT) check placement
 - Inject 10 ml of air with a 60 ml syringe into the NGT while listening over the left upper quadrant for air entering the G.I. tract
 - Check placement of NGT every 4 hrs by checking for residual using a 60 ml syringe aspirate stomach contents
 - NOTE: insufflation of air alone is not sufficient to verify tube position since auscultation over the stomach can pick up sounds transmitted from the bronchial tree. Aspirated stomach contents indicates that the NGT is in the stomach
- NGT drainage quantity/character/color/guiac/pH
- Jejunostomy tube (JT) patent
- Feeding tolerance/nutritional status
- Bowel sounds 4 quadrants
- Bowel movements character of stool, guiac
- Rectal bag

GU

- Foley catheter:
 - Indwelling catheters are the primary cause of UTIs!!
 - Strict hand washing and gloves when manipulating foley catheter
 - Foley Catheter-secure device in place
 - Foley catheter tubing free of kinks
 - Collection bag below bladder and off the floor
 - Empty collection bag when half full
- Urine quality, color
- BUN/Creatinine

• Hourly output/I and O/weight daily

Skin

- Color, texture, turgor, temperature
- Rashes, abrasions, wounds, burns, bruises, inflammations
- Status of bony prominences
- Incisions
- Decubitus
- Wounds/drains/dressings
- Cyanosis/mottling
- Evaluate need for specialty mattress and splints

IV Access

- Assess IV sites
- Identify your infusions and trace tubing from patient back to Intravenous pump
- Identify medication/dosage/rate
- IV bags and syringes (on syringe pumps) have correct medication labels, check to see how much is left to infuse (you may need to mix another bag)
- Compatibility of drugs infusing in same line
- IDENTIFY YOUR IV PUSH LINE

OCCUPATIONAL AND PHYSICAL THERAPY

BHAKTI K. PATEL, MD • JOHN P. KRESS, MD

ICU Acquired Weakness (ICU-AW)

Definitions

- Generalized symmetrical weakness ranging from paresis to true quadriplegia sparing the facial muscles (Chest. 2007;131:1541)
- Electrophysiologic testing and histology defines additional categories of ICU-AW
 - Critical Illness Polyneuropathy (CIP) diffuse and symmetric axonal neuropathy manifested typically by distal motor and sensory deficits with normal distal tendon reflexes (Clin Chest Med. 2006;27(4):691)
 - Critical Illness Myopathy (CIM) acquired primary myopathy clinically recognized by proximal muscle weakness without sensory deficits and decreased or absent reflexes (Curr Opin Crit Care. 2007;13(5):489)

Causes

- CIP
- CIM
- Immobilization leading to disuse atrophy and deconditioning

Epide miology

- Neuromuscular weakness is prevalent in 46% of adult ICU patients with sepsis, multiorgan failure, or prolonged mechanical ventilation (Intensive Care Med. 2007;33:1876)
- Risk factors for ICU acquired weakness
 - Female sex, number of days with multiorgan dysfunction, prolonged mechanical ventilation prior to awakening, corticosteroid administration (JAMA. 2002;288(22):2859)
 - Inflammatory states (e.g., sepsis, SIRS), neuromuscular blockade, hyperglycemia

Diagnosis

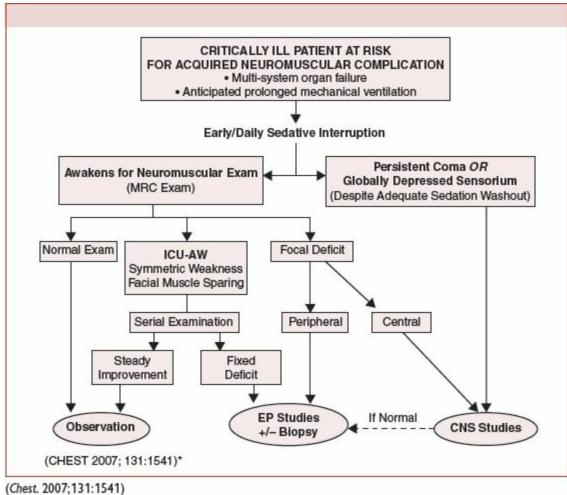
- ICU acquired weakness is recognized in two clinical scenarios
 - Difficulty in liberating a patient from mechanical ventilation
 - Profound persistent weakness despite return of sensorium
- Electrophysiological evaluation
 - A reduced amplitude of the compound muscle action potential (CMAP) and sensory nerve action potential (SNAP) measure conduction velocity and amplitude of the sural SNAP and peroneal CMAP in one leg, using surface stimulation and recording electrodes
 - If SNAP or CMAP decreased by more than 25% on two consecutive days, a complete electrophysiological test should be performed (Critical Care. 2007;11:R11)
- Medical Research Council (MRC) Score
 - Strength testing of three muscle groups in each limb on a scale of 1–5
 - Assess function when sedation is interrupted:

- Upper extremity: wrist flexion, forearm flexion, shoulder abduction
- Lower extremity: ankle dorsiflexion, knee extension, hip flexion
- ICU-AW defined as an MRC score <48 (JAMA. 2002;288:2859)

MRC: Muscle Examination Score for Each Movement	
0 - No visible contraction	
1 – Visible muscle contraction, but no limb movement	
2 - Active movement, but not against gravity	
3 – Active movement against gravity	
4 - Active movement against gravity and resistance	
5 - Active movement against full resistance	
Maximum score: 60 (15 pts per limb) and Minimum score: 0 (quadriplegia)	

• Diagnostic algorithm for ICU-AW

Figure 1. Proposed Algorithm for Assessing Neuromuscular Complications in the Critically Ill



EP, electrophysiology; +/-, with/without.

Consequences

- Prolonged mechanical ventilation
- Increased ICU length of stay
- Increased in-hospital mortality

Prevention and Treatment

- Electrical Muscle Stimulation
 - Daily EMS is performed simultaneously on the quadriceps and peroneus longus muscles of both lower extremities
 - After leg shaving and skin cleaning, place rectangular electrodes on the quadriceps and peroneus longus muscles of both legs
 - Stimulator is set to deliver biphasic, symmetric impulses of 45 Hz, 400 sec pulse duration (12 sec on and 6 sec off), at intensities able to cause visible contractions
 - Duration of the session is approximately 1 hr
- Clinical Outcomes of Electrical Muscle Stimulation (Critical Care. 2009;13:R161; Critical Care. 2010;14:R74)
 - Preservation of muscle mass in stimulated muscles compared to control
 - Reduced incidence of ICU-AW by MRC score (12.5% vs. 39.3, p = 0.04)
 - Improved overall MRC scores (58 vs. 52, p = 0.04)
- Intensive insulin therapy (NEJM. 2006;354:449) (NEJM. 2001;345:1359). While this is no longer recommended practice, due to the high incidence of hypoglycemic episodes, good glucose control (keeping blood glucose below 160–180 mg/dl) is essential for good outcomes.
 - Tight glycemic control was associated with decreased incidence of critical illness neuromyopathy in medical (38.9% vs. 50.5%, p = 0.02) and surgical (28.7% vs. 51.9%, p = 0.001) patients in the ICU for ≥ 7 d
 - Intensive insulin therapy was protective against critical illness neuromyopathy (Neurology. 2005;64:1348) (Am J Respir Crit Care Med. 2007;175:480)
- Early mobilization (see below)

EARLY MOBILIZATION

Definition

- Initiation of physical activity at the time of initial physiologic stabilization and continuing throughout ICU stay (Crit Care Med. 2007;35(1):139)
- May occur as early as 1.5 d after endotracheal intubation/ICU admission (Lancet. 2009; 373:1874–1882; Crit Care Med. 2010;38:2089)

Initiation of Early Mobilization (Crit Care Med. 2010;38:2089)

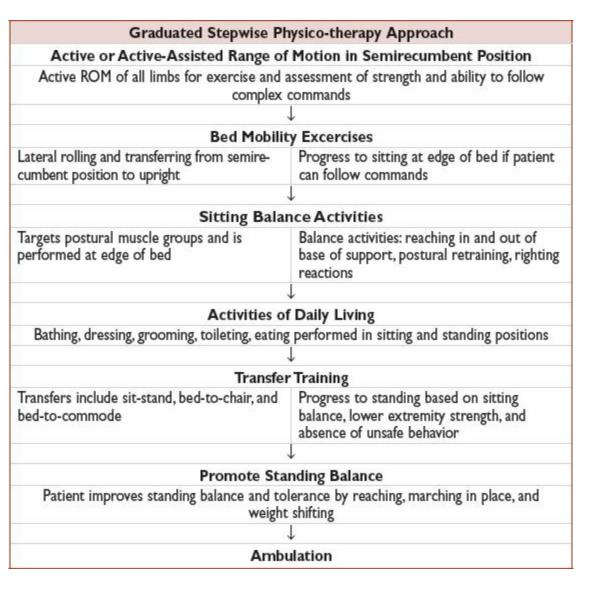
- Perform daily interruption of sedation unless neuromuscular blocking agents are being given or severe agitation is present (also see Chapter 8)
- Assess for contraindications for initiating physical and occupational therapy, these are:
 - Mean arterial pressure < 65
 - Heart rate < 40, >130 beats/min
 - Respiratory rate < 5, >40 breaths/min
 - Pulse oximetry < 88%
 - Evidence of elevated intracranial pressure
 - Active gastrointestinal blood loss
 - Active myocardial ischemia
 - Actively undergoing a procedure
 - Patient agitation requiring increased sedative administration in the last 30 min
 - Insecure airway (device)
- If no contraindication to early mobilization present, "wakefulness" is assessed during daily

interruption of sedation (DIS)

- "Wakefulness" demonstrated when the patient is able to follow at least 3 of 4 commands: opening eyes, using eyes to track, squeezing hand, and protruding tongue on request
- If patient is unresponsive after DIS, passive range of motion (PROM) exercises are performed on all 4 limbs
- If unresponsiveness persists for >6 hrs then a second session of PROM should be performed
- If "wakefulness" present, therapy should be delivered by a team consisting of a physical and occupational therapist. ICU nursing and physician staff should coordinate efforts for screening and safety for therapy sessions

• Preparing for therapy session

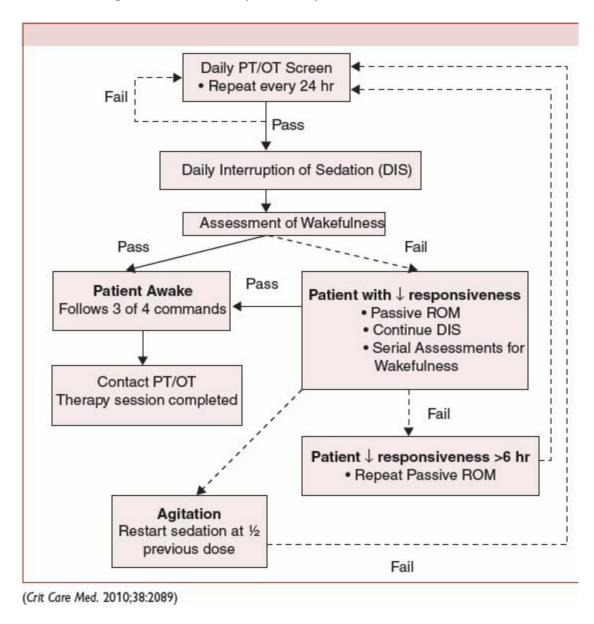
- All devices (vascular access catheters, enteral tubes, endotracheal tubes) must be assessed and secured
- Any unnecessary noninvasive devices should be removed (pneumatic compression stockings, etc...) and enteral feedings should be stopped
- All equipment should be moved to the side of the bed where the mechanical ventilator is located. Similarly, the patient should be mobilized to that side of the bed
- If ambulation is anticipated, a transport ventilator should be present



- Contraindications to continuing of physical and occupational therapy:
 - Mean arterial pressure < 65

- Heart rate < 40, >130 beats/min
- Respiratory rate < 5, >40 breaths/min
- Pulse oximetry < 88%
- Marked ventilator dyssynchrony
- Patient distress (nonverbal cues or physically combative)
- New arrhythmia
- Concern for myocardial ischemia
- Concern for airway device integrity
- Fall to knees
- Endotracheal tube removal

Figure 2. Summary of Early Mobilization Protocol



Clinical Outcomes of Early Mobilization (Lancet. 2009;373:1874; Crit Care Med. 2008;36:2238; Crit Care Med. 2009;37:2499)

- Increased return to independent functional status at hospital discharge (59% vs. 35%, p = 0.02)
- Shorter duration of delirium (2.0 vs. 4.0, p = 0.02)
- Increased ventilator free days (23.5 d vs. 21.1 d, p = 0.05)
- Improved ICU length of stay 5.5 vs. 6.9 d (p = .025)

- Improved hospital length of stay 11.2 vs. 14.5 d (p = 0.006)
- Improved 6 min walking distance (196 vs. 143 meters; p < 0.05)
- Improved subjective feeling of functional well-being (as measured with "Physical Functioning" item of the Short Form 36 Health Survey questionnaire) (21 vs. 15 points; p < 0.05)
- Improved isometric quadriceps force

TRANSITIONING FROM ACUTE CARE TO REHABILITATION

SHANNON S. MCKENNA, MD

THE NEED

An increasing number of patients survive acute critical illness with significant disability and ongoing organ system dysfunction. Factors contributing to this trend:

- Increasing age
- Increasing complexity of treatment
- Decreased mortality from sepsis, ARDS and cancer

If these patients are cared for at the acute care facility for the entire duration of their illness, ICU beds are occupied by long stay chronically critically ill patients. The result:

- Patients are "boarded" in the PACU or ED when ICU beds are in short supply
- ED may have to go on diversion
- Newly critically ill patients experience delays in receiving definitive critical care, which may worsen outcomes

Reimbursement patterns and limited acute care beds have driven the development of post acute care facilities

Types of Post Acute Care Facilities

Broadly classified as long-term acute care (LTAC), inpatient rehabilitation, and skilled nursing facilities (SNF)

- LTAC: average length of stay >25 d; complex medical management including ventilator weaning and dialysis; daily physician assessment and the availability of specialty consultation; IV medication administration; wound care; intensive rehabilitation therapy (PT, OT, speech therapy) is available for patients able to participate
- **Inpatient rehabilitation:** intense rehabilitation is primary need; ongoing medical management is a secondary concern
- SNF: low complexity medical needs not requiring daily physician visits; less intense rehab needs or not able to participate in intense rehab program

Most patients being discharged directly from the ICU will require LTAC level care

OUTCOMES

• Paucity of data available

- Study of Medicare patients >64 y/o transferred from ICU to a LTAC between 2004 and 2006 found: 27% discharged home, 35% discharged to SNF, 14% transferred back to acute care facility, and 23% died. 1 yr post-admission mortality was 52% (JAMA. 2010;303:2253)
- Overall 1 yr survival of patients requiring prolonged mechanical ventilation about 50% (multiple studies)

EVALUATING PATIENTS FOR SUITABILITY OF TRANSFER TO AN LTAC

Each patient should be evaluated for the suitability of transfer. Those who are unlikely to do well at an LTAC should not be transferred even if bed availability issues are critical

Triage Criteria f	or Patient Transfer
Appropriate for Transfer	Not Appropriate for Transfer
Hemodynamically stable	Hemodynamically unstable
On stable medication regiment	Likely to need urgent physician assessment
Tracheostomy in place if ventilated; not requiring continuous IV sedation	Likely to need complex diagnostic work-up (MRI, CT, etc.)
Dressing changes (if needed) BID or less	Likely to need urgent therapeutic interven- tions (bronchoscopy, etc.)
Permanent feeding tube and IV access in place (if needed)	Requires suction more than q2h (may vary by facility)
Hemodialysis on 3 times a week schedule	Agitated delirium requiring 1:1 sitter (unless facility can provide)
Organ system failures persistent but stable	Worsening organ system failure
	Terminal illness with little chance of recov- ery (LTAC is not a hospice)
	Low complexity medical needs – inpatient rehab or SNF more appropriate

STEPS TO ENSURING A SUCCESSFUL TRANSFER

Know the Facility

- What is the staffing pattern, what services are available on site, how are urgent situations handled, how much rehab can be provided
- Create a means for regular follow-up. Discuss which patients did well at the facility and which did not. What can be learned for the future from past experiences?
- Partnering with a single facility, or a small number of facilities, is likely to increase the success of transfer.

Prepare the Patient and Family

- Staffing is different at LTACS routine care may be provided by assistants (bathing, vitals), RNs are not continually in sight, physician contact time may be less. Patients and families should expect to be somewhat anxious for the first few days in a new environment. Discuss this up front. Emphasize that "different" doesn't mean "bad".
- Some patients will transfer back and forth between the LTAC and acute care several times. Patients and families should be prepared for this and not see it as a failure of the LTAC.

- Make sure appropriate airway, enteral, and IV access are in place as needed
- Adjust medication routes/schedules: enteral when possible, batch administration times together, avoid middle of the night doses
- Establish stable bowel regime
- Remove any tubes, catheters, drains, staples, or sutures that can be removed before transfer

Communication

- Focused but complete sign out to the care team at LTAC prevents the need to "reinvent the wheel". Verbal sign outs between physicians, nurses, respiratory therapists, and physical therapist rapidly identify the unique features and needs of a given patient
- Detailed written summaries should accompany the patient to add to and reinforce the information given verbally
- Provide a person/number to call 24 hrs a day if the facility has questions about the patient. Timely contact may allow appropriate treatment of known problems to be initiated at the LTAC without transfer back to acute care

PATIENT- AND FAMILY-CENTERED CARE

MARY PENNINGTON, RN, MSN, CCRN • PATRICE K. NICHOLAS, DNSC, DHL (HON.), MPH, MS, RN, ANP, FAAN

The national patient safety movement, regulatory agency directives, patient advocacy groups and a growing complexity in technology and therapeutics have created the impetus for a paradigm shift towards patient and family centered care especially in the intensive care units

DEFINITIONS

- Patient- and family-centered care: a partnership among physicians, nurses, other providers. Clinical decisions made are congruent with the patient's wants, needs and preferences. Patients and families are encouraged to participate in their own care and decision-making. (IOM. 2001b, p. 7)
- Family-centered care: takes patient-centered care and widens the circle of concern to include the family. This is a holistic model of care based on the concept that patients are part of a larger 'whole' that defines them and must be integrated into the healthcare team

OBJECTIVE

- Doctors and nurses respect and understand patients' values, preferences and cultural beliefs
- Patients and families are included in the plan of care and are informed and actively involved in medical decision-making
- Patient care is coordinated and communicated among all healthcare providers participating in the patient's care
- The physical comfort and emotional support of patients and family members is a priority for all members of the healthcare team

RATIONALE

Directives from professional organizations, regulatory bodies, and consumer advocacy groups:

- The Joint Commission, Institute of Medicine, Society for Critical Care Medicine and the Association of Critical Care Nurses are in consensus that quality healthcare must be safe, patient-centered, culturally focused, and equitable
- The American Nurses Association's (*ANA*. 2001) Code of Ethics for Nurses central ethical tenet directing the nursing profession is respect for persons and supporting their value systems across the health-illness continuum. This extends and encompasses the nurse's commitment to the patient, whether an individual, family, group, or community. American Nurses Association Social Policy Statement: nursing includes the advocacy in the care of individuals and families as well as communities and populations (ANA. 2003).

- Directives from Professional Organizations:
 - The Society of Critical Care Medicine (SCCM) has developed models to improve patient- and family-centered care in critical and intensive care units. (website: www.sccm.org)
 - Institute of Healthcare Improvement (IHI) has developed a patient- and family-centered approach that includes the development of an action plan to advance meaningful partnerships with patients and families in hospitals including in critical/ intensive care settings. The IHI has developed a Patient- and Family-Centered Care Organizational Self-Assessment Tool (website: www.ihi.org).

KEY CONCEPTS

- Largest volume of patient/family dissatisfaction relates to poor communication and restricted access to patients
- Increased and flexible visitation for patients and families are associated with improved outcomes and satisfaction
- Visitation policies must be highly individualized to meet the needs of the patient and family as well as the unit
- Families of critically ill patients experience challenges that are unique to each family and may produce disruption in family functioning that are linked to crisis-like behaviors that include confusion, shock and intense fear. Anxiety, anger, sadness, and resignation may occur in the family. However, enhanced patient- and family-visitation may limit the negative effects of a critical/intensive care stay for the patient
- Family members often do not pay attention to their own needs and healthcare providers underestimate the complex needs of family members

Families have essential needs in the critical/intensive care settings: information, reassurance, proximity to the patient

PATIENT- AND FAMILY-CENTERED CARE INTERVENTIONS

COMMUNICATION

- Providing ongoing information to families is an important priority
 - Keep explanations brief and clear
 - Early, accurate and in terms that families can understand (try to use wording at the 9th grade level of comprehension).
 - The need for hope is universal
 - Family members place great importance on being called at home if the condition of the patient changes
 - Avoid misunderstandings: reiterate facts
 - Structured communication in the form of regular and shift-by-shift contact
 - Family members have a need to speak to a physician at least every day regarding the condition of and the prognosis for the patient

- Involving the family in patient rounds at each round is critical
- Daily and post-morning round telephone calls to update the family
- Family meetings with the identified family contact person each day, if needed
- What to expect after hospitalization
- Alternatives to treatment (Davidson. Critical Care Medicine, 2009;35:605–622.)
- Patient- and family-centered care requires that a nurse explain to them about the care, the unit, the equipment and what the families can do for the patient when visiting. Families often feel helpless and appreciate participating in care
- Opportunities must be established for patients/family to state their goals
- ICU Family Information booklets must be readily available for families:
 - Provide concrete information about the ICU, work flow, technology
 - Write names ICU physician, nurse, social worker in the booklet for the family
- Daily reviews with family members are essential in establishing the routine and plan with the family: always ask if they have questions/concerns
- Encourage family to bring in familiar objects, picture, and mementos that have meaning to the patient and family
- Shared Decision Making:
 - Family assumes the voice of the patient in helping to make decisions for incapacitated individuals
 - Families may feel burdened when asked to be solely responsible for making decisions
 - Highly emotional and/or crisis states
 - Complexity of medical diagnosis
 - Prognosis uncertainty
 - ICU team shares accountability with families in a true partnership for decisions made
 - Decreases family anxiety
 - Allows patient preferences to be identified.

FLEXIBLE VISITATION POLICY

Allows the family to visit any time, as often as they desire and for as long as they wish (unless the patient requests no visitors)

- Improves family and patient perceptions of the quality of care
- Reduction of anxiety of the patient:
 - Less likely to worry about family members when they can see them often
 - Patients feel loved and more secure when they have more frequent visitors
- Family members are more satisfied with a liberal visitation policy:
 - Allows them to visit at times that are more convenient for them
 - Other responsibilities may limit when they can visit
 - May live long distances from the hospital and can see the patient when they arrive
- Family members report less exhaustion with an open visiting policy
- Restriction to visiting is at the discretion of the nurse:
 - If there is an emergency on the unit
 - If their presence is detrimental to the patient

"Visitation in Critical Care: Processes and Outcomes of a Performance Initiative," Roland et al. (2001)

65% indicated that more open visitation was desirable

90% felt that visitors were very important to them

85% stated the desire that family perform personal care for them

75% denied feeling fatigued after visiting.

FAMILY'S LEVEL OF INVOLVEMENT

- Families come with specific and unique strengths, limitations, characteristics, challenges, and skills
- Assess individually to determine capacity and desire regarding participating in care and develop and individualized plan of care for each patient and family
- Important to be aware of the psychosocial issues present that may influence how family members react or involve themselves in the patient's care

FAMILY PRESENCE DURING CODES

Evidence suggests that the majority of families (60%–80%) would be at their loved one's bedside during CPR if given the option (AACN News. 2004)

Family Member Presence During CPR

- Removes doubt, know everything done
- Reduces anxiety and fear
- Supports and helps patient: active role
- Sustains patient-family connectedness and bonding
- Facilitates closure
- Facilitates grief process
- No adverse psychological effects among families at follow-up

Patients

- Almost universally, children want parents present
- Reports from adult patients
 - Felt comforted, less scared, less alone, safer, able to better cope with event
 - Poor communication and restricted access during CPR were identified as among the most stressful aspects of care and recovery for family members.

CULTURAL ISSUES

- Culturally competent care: physicians, nurses, other healthcare team members mirror the multicultural backgrounds of the patient population
- Clashes between patients/families and healthcare providers can occur when cultural differences and values are not understood. Consult from ethics service, patient and family relations, social work, and/or chaplaincy

- To understand and support patients and their families during the crisis of critical care admission, knowledge of differences in cultures is essential
- 'When the needs of patients' families are met, families are better able to cope with the ICU environment, clinical trajectory and contribute to the patient's care during and after discharge.

ETHICS AND PALLIATIVE/END OF LIFE CARE

MICHAEL F. O'CONNOR, MD • DANIEL J. RUBIN, MD

- Palliative Care is the prevention or treatment of suffering in dying patients
 - Represents a change in focus from treating the disease to alleviating its symptoms
 - Emphasizes the importance of comfort for the patient and access for family and friends during the dying process
 - The critical care team provides emotional support for the family and patient
 - Palliative care is initiated when the patient or family has decided to discontinue curative treatment of the terminal illness
- Ethical issues in the ICU (Crit Care Med. 2007;35:S85)
 - Patient autonomy is of primary importance when establishing goals of care
 - Capacity: The understanding that patients have the ability to make decisions for themselves based on an understanding of their condition, prognosis, treatment options, and they are able to participate in the process of informed consent
 - Patient Self-determination Act passed in 1990
 - Right to participate and direct their own healthcare decisions
 - Right to refuse or accept medical interventions
 - Right to prepare advance directive
 - Right to obtain specifics about provider's policies governing the rights of an advance directive.
 - The "Surrogate" or "Proxy" makes decisions that should represent the patients values and wishes once the patient has lost capacity
 - The **best interest principle** guides the surrogate or proxy to make decisions with the best interests of the patient given the patients values and wishes
 - Paternalism gives physicians a moral basis for the ability to compromise a patient's autonomy to promote the patient's welfare
 - Advance Directives help establish the patient's wishes when they are incapacitated
 - Instructional documents, such as a living will, establish the treatments that the patient would accept or refuse if they become incapacitated
 - Some states do not recognize these documents as legally binding
 - A health care proxy or durable power of attorney is a legally binding document that designates a surrogate by the patient to make treatment decisions based on the patient's wishes if they become incapacitated
 - Power of attorney is valid any time the patient is incapacitated
 - Patients without a designated surrogate should have either a court appointed guardian or an ethics committee review to determine the goals of care
 - Statute in some states (e.g., Illinois) can designate POA, typically nearest competent living relatives
 - Beneficence is the moral obligation to promote goodness or benefit to the patient and family, provide care that maintains or improves health, reduces disability, and alleviates physical, and existential, pain and suffering

- Physicians are ethically bound to not injure patients (nonmaleficence).
- Establishing Goals of Care (Crit Care Med. 2008;36:953)
 - Physicians should clarify goals of care with the family: Restoring health, extending life, alleviating pain and suffering
 - Communicating to the family realistic expectations about whether the goals of care can be achieved with the current treatments is essential to resolving conflict
 - Physicians are not obligated to provide treatment to patients that they believe cannot achieve the goals of care as defined by the family and physicians
 - Physicians are not obligated to provide care they deem futile
 - Mediation by a hospital ethicist may be beneficial at this time
 - There is no legal distinction between extraordinary vs. ordinary treatments such as mechanical ventilation vs. nutrition and hydration
 - Medical interventions should be evaluated by weighing the benefits and burdens they confer to the patient
 - Therapy should always be focused on whether they will accomplish the goals of care
 - Treatment that merely prolongs the dying process should be eschewed

• Withdrawing vs. Withholding care

- Three ethical principles guide the withdrawal of life-sustaining care in the United States
 - Philosophical and legal analyses do not differentiate between withholding or withdrawing care
 - The withdrawal of life-sustaining care is not legally considered murder
 - The actions of the physician during withdrawal of care are considered to allow the patient to die from the underlying illness
 - The "double effect principle" allows a physician to treat a patient's pain even though it may hasten the dying process
 - Pain medication given with the intention to make the patient comfortable is acceptable even if it hastens death
- Practical aspects of withdrawing care
 - The goals of withdrawing care for the patient are
 - Provide adequate pain management
 - Avoid undesired prolongation of dying
 - Allow the patient to sustain a sense of control
 - Continuous monitors should be masked or discontinued to ensure the family focuses on the patient and not alarms or numbers
 - Discontinue labs/tests not benefiting the patient
 - Decision to withdraw care made: should take place in the current room of the patient if it does not frustrate care of other patients
 - Allow Family members to stay with the patient during dying process
 - Sedatives and Analgesics (Crit Care Med. 2008;36:953)
 - Alleviate pain, dyspnea and other distressing symptoms
 - Opioids for treatment of pain and dyspnea; titrated to patient comfort
 - Patients undergoing withdrawal of care may not be able to report their pain
 - Physiologic variable and behavioral observations may be best gauge of pain
 - Tachycardia, tachypnea, fearful facial expression
 - Benzodiazepines are mainstay for anxiolysis, amnesia and sedation
 - They do not have any analgesic properties

		Opioid Ar	nalgesic Ag	ents		
Opioids	Equivalent Dose, IV ^a	Onset to Peak Effect, mins	Duration of Effect, hrs	Typical Adult Dose, IV	Typical Pediatric Dose, IV	Typical Infusion Rate
Morphine	10 mg	20–30	3–4	2–10 mg	0.1 mg/kg	0.05-0.5 mg·kg-1·hr-1
Fentanyl	100 mcg	2–5	0.5–2	0.5–2 mcg/kg	1–5 mcg/ kg	0.5-10 mcg·kg ⁻¹ ·hr ⁻¹
Hydromorphone	1.5-2 mg	20-30	3–4	0.5-2 mg		

IV, intravenous

"Equivalent doses are approximations and are of limited value due to differences in onset and duration of effect. (Crit Care Med. 2008;36:953)

			Sedative Age	nts		
	Onset to Peak	Duration		l Initial Oose	Typical Infusio	
	Effect, mins	of Effect, hrs	Adult	Pediatric	Adult	Pediatric
Sedatives Lorazepam	20–25	2–4	1–3 mg	0.05 mg/kg	0.5–4 mg/hr	0.05-0.1
Midazolam	5–10	1.5–2	0.02–0.1 mg/kg	0.1 mg/kg	1–5 mg/hr	mg·kg ⁻¹ ·hr ⁻¹ 0.05–0.1 mg·kg ⁻¹ ·hr ⁻¹
Propofol	1–2	0.1-0.4	1 mg/kg	1 mg/kg	10-50 mcg· kg ⁻¹ ·min ⁻¹	10-50 mcg kg ⁻¹ -min ⁻¹
Neuroleptics Haloperidol	25–30	2–4	0.5–20 mg	_	3–5 mg/hr	-

IV, intravenous. (Crit Care Med. 2008;36:953)

- Once the patient has died communication should use simple and unambiguous language stating the patient has died
- Reassure family that appropriate care and decisions were made

INTER AND INTRA-HOSPITAL TRANSPORT OF CRITICALLY ILL PATIENTS

MICHAEL G. FITZSIMONS, MD • CHONG NICHOLLS, MD

DEFINITIONS

- Inter-hospital transport (secondary transport) involves the transport of a patient between two hospitals. The reasons for such transport vary between hospitals, healthcare systems, and countries
- **Intra-hospital transport** involves the movement of a patient throughout the same hospital for care and procedures that cannot be performed at the bedside

During transport the patient's physiologic functions should be supported and monitored to the same degree they were before transport.

RISKS AND BENEFITS

There are no absolute contraindications to patient transport other than refusal by a competent patient. Conditions where the transport of an unstable patient is desirable, may include transfer for angiography and embolization of a bleeding patient, or transfer to the operating room for the same.

Relative Contraindications to Patient Transport

Hemodynamic instability Inability to oxygenate or ventilate Inadequate personnel

Note: These contraindications are relative and they would not be in effect in the purpose of the transport is to treat the underlying cause of the physiological derangement

- Benefits. Transport within the hospital results in a change in patient management in 24%–39% of travels (*J Trauma*. 1992;33:582 and *J Trauma*. 1988;28:1020).
- Risks. Hemodynamic or respiratory compromise may occur in up to 68% of patient transports, but all organ systems may be affected (*J Trauma*. 1988;28:1020).
 - Hemodynamic changes and risk
 - **Hypertension or hypotension** may occur in up to 50% of transports (*Am J Crit Care*. 1995;4:106). Factors such as emergence from anesthesia, manual ventilation, pain, stress, and anxiety contribute
 - Arrhythmias are more commonly seen in patients transported after myocardial infarctions
 - Respiratory changes and risks
 - **Hypoxemia** is more likely to occur in patients receiving mechanical ventilation, needing higher levels of positive end-expiratory pressure (PEEP), and higher levels of oxygen support (FiO₂) (*Intensive Care Med.* 1995;21:784).

- **Hypoventilation and respiratory acidosis** may worsen intracranial pressure and pulmonary hypertension
- **Hyperventilation and respiratory alkalosis** may worsen acute head injury or impair venous return and cardiac output
- Patient subject to transport may have an increased risk of **pneumonia** due to aspiration
- Transport is a risk factor for accidental extubation (*J Clin Anesth.* 1996;8:289).
- Temperature alteration
 - Transport often requires the interruption of active fluid warming and warming blankets resulting in **hypothermia**. Hypothermia may worsen acidosis, coagulopathy, myocardial performance, and arrhythmias
 - Relative **hyperthermia** may be a risk in patients subject to active cooling (head injury)
 - Risk factors for hypothermia include children, elderly, spinal injury, and burn victims
- Injury
 - Transport risks displacement of fractures, chest tubes, pacing wires, and central lines, and may worsen cervical spine injury
 - Transport risks injury to the health of care providers
 - Transport involves the transfer, lifting, and turning patients
 - A significant percentage of nurses leave the profession or move to less demanding jobs due to **back injuries** associated with patient transport (*Int J Nurs Stud.* 1986;325)

ASSESSMENT AND PREPARATION

- Assessment
 - General assessment
 - Patients demonstrating more respiratory and hemodynamic instability prior to transport are more likely to have problems en route (*Pediatrics*. 1989;84:43; *Crit Care*. 1999;3:R83).

Pat	ient Assessment and Preparatio	n
Airway	Breathing and Oxygenation	Circulation
Endotracheal tube (ETT) position Adequacy of ETT function Cervical spine control	Mode of ventilation Tidal Volume Respiratory rate PEEP FiO ₂ SpO ₂ Need for muscle relaxation Presence of pneumothorax	Blood pressure Heart rate Cardiac rhythm Hemodynamic support

• Airway

- Certain patients may benefit from endotracheal intubation prior to transport
- Medical conditions and patient populations potentially benefitting from intubation prior to transport
 - Hypoxemia, burn injury, cervical spine injury, combative patients, anaphylaxis, epiglottitis, laryngotracheal trauma, facial fracture, neurologic compromise, significant hemodynamic instability
- Consent, Records, and Communication

- Written consent should be obtained from the patient or healthcare proxy before transport to another facility, if possible (*Crit Care Med.* 2004;32:256).
- Copies of all **relevant medical records** and studies should accompany patients during transport within a hospital or between hospitals.
- There must be **direct verbal communication** between the physician initiating a transfer and the physician that will ultimately receive the patient. Early communication may allow the transferring facility to establish monitoring or perform other interventions that the receiving facility deems necessary.

MONITORING PATIENTS DURING TRANSPORT

- No widely accepted national standards exist for patient monitoring/equipment during transport, although guidelines do exist (*Crit Care Med.* 2004;32:256)
- Equipment must be compact, lightweight, must be portable with audible and visible alarms, easy to read monitors, and have a long battery life
- In general patients should be transported with the same level of monitoring as they have in the originating location
- Cardiovascular monitoring
 - All critically ill patients need **electrocardiogram (ECG)** monitoring, non-invasive (or invasive) blood pressure monitoring, pulse oximetry (see Chapter 2), manual or portable mechanical ventilation (if require ventilatory assist).

Infusion Devices

Most critically ill patients are transported while receiving continuous infusions

- New "**smart pumps**" have many characteristics designed for safe operation including preprogrammed drug libraries, high and low "lock-out" rates, visible and audible alarms, free-flow prevention, and occlusion alerts
- All transporting personnel must be familiar with safe operation and routine trouble shooting of such devices
- All hospitals and hospital systems should require that equipment be consistent among different locations to avoid unfamiliar devices

GROUND AND AIR TRANSPORTATION

Transportation via ground (ambulance) or air (rotor wing or fixed wing)

- Ground transportation by ambulance has several advantages over movement by air
 - The skill level of team involved in ground transport must be known before the decision is made to move a patient
 - Some transport systems rely upon individuals trained in basic life support (BLS) only, others deploy personnel trained in advanced cardiac life support (ACLS), while some are staffed by fully trained physicians or highly skilled critical care transport teams

• **Transport by air** is beneficial for distances greater than 45 miles when compared to ground (J *Trauma*. 2005;58:148).

Comparison of Fixed	versus Rotor Wing Transport	
Fixed Wing (Airplane)	Rotor Wing (Helicopter)	
Long-distance capability (>250 miles)	Better for distances <250 miles	
Requires landing strip	Vertical take off	
Larger patient care area	Limited space for care	
Transport of several patients	Limited patient number (1-2)	
Less noise and vibration	More noise and vibration	
Requires higher altitude	Transport at lower altitude	
Longer mobilization times	Rapid mobilization	
Airport based	Hospital based	

- Factors to consider in air transport
 - Risk of hypoxemia with transport at altitude
 - Expansion of gases within a closed cavity (gastric distension, expansion of pneumothorax, pneumopericardium, etc.) (*Crit Care Clin.* 2000;16:695).
 - Effect of altitude on equipment such as blood pressure cuffs, endotracheal tubes, ventilators) (*Crit Care Clin.* 2000;16:695).
 - Drying of secretions
 - Limited mobility of care provider
 - Effect of vibration, acceleration, deceleration on patient comfort and injuries

OPERATING ROOM: CARING FOR THE EXTREMELY CRITICALLY ILL PATIENT

EMILY NELSON, MD • GYORGY FRENDL, MD, PhD

Key elements:

- A rapid but thorough pre-operative assessment of the acute process and associated organ dysfunctions
- Understanding the patient's preexisting co-morbidities and their degree
- Focus on the timely identification and management of the most life-threatening conditions
- Deployment of strategies to prevent worsening of the patient's condition while providing a chance to improve (in order to complete the most needed portions of the operation)
- Examples:
 - Applying lung-protective ventilation for a patient with inhalational injury, aspiration, or lung contusion
 - Switching to "damage control surgical management" for trauma patients when the anesthesiologist notices the development of the "triad of death: acidosis, hypothermia, hypercoagulability"
- Deployment of interventions to restore/replace vital organ function. Examples:
 - Deployment of renal replacement therapy (i.e., CVVH) in the OR for a burned or septic shock patient with acute renal failure who is also suffering from severe fluid overload, intractable acidosis or a life threatening electrolyte imbalance
 - Placement of a pulmonary artery catheter with pacing ability to allow urgent surgery for a patient who suddenly developed third degree AV nodal block

PRE-OPERATIVE ASSESSMENT OF THE SEVERELY CRITICALLY ILL PATIENT SHOULD FOCUS ON

- A rapid but thorough assessment of the acute process and associated organ dysfunctions
- Understanding the patient's preexisting co-morbidities and their degree

Specific organ systems should be evaluated for the following concerns:

- *Neuro*: Determine and document the patient's pre-injury mental status and basic neurological exam, the changes the injury has caused, as well as any focal deficits. Assess if the patient is sufficiently sedated, and if his/her pain is treated. Plan to perform a neurologic exam at the end of the operation.
- *Cardiovascular*: Assess the patient's hemodynamic condition. Look for recent echo results: abnormalities in EF, pulmonary pressures, and valvular disease. Is the patient pressor dependent? Be aware of escalating doses. History of coronary disease or recent MI or arrhythmias? If the patient has a pacemaker/ICD, ask what kind and when it was last interrogated, or if ICD has fired recently. Patients with ventricular assist devices (VAD) may need non-cardiac surgical interventions. Assess volume status. Beware of cardiac contusion causing RV dysfunction or AV

block.

- *Pulmonary:* Assess the status of lungs (use CXR, chest CT, ABG). Note preop ventilator settings and FiO₂. Evaluate if the patient will likely require transport ventilator to and from the OR or ICU ventilator during the procedure. Look for history of signs of chronic and/or acute pulmonary hypertension.
- *Airway:* Quickly assess airway for intubation (beware of C-spine injury, if unknown keep spine precautions). If the patient has been intubated, document if it was a difficult intubation; if trached, document when it was performed. What size ETT and type/size of tracheostomy tube is in place (cuffed or uncuffed assess need to replace uncuffed trach)?
- *Renal/electrolytes*: Does the patient have abnormal renal function? If in ESRD, when was last dialysis? What are most recent electrolyte values? Does the patient have an acidosis?
- *Heme*: Is the patient actively bleeding? Does the patient have a coagulopathy and why? Document most recent Hct, platelets, and coagulation parameters. Ask for a type and cross to be performed, and ensure that blood is readily available (be aware of the presence of antibodies in the recipient's serum as they will make cross match more prolonged and difficult).
- *GI*: Confirm NPO status or the lack thereof. Trauma patients should be assumed to be full stomach and be intubated with rapid sequence intubation. Is the patient on TPN or should a CVC port be saved for TPN? Is the patient on tube feeds?
- *Endo:* Check and manage blood sugars, keep in the 120–180 mg/dl range. Look for chronic steroid use.
- *ID*: Provide appropriate perioperative antibiotic coverage. If the patient is septic early, broad spectrum antibiotic administration has significant benefits.
- Musculoskeletal: Rule out recent orthopedic injuries or myopathy.
- Derm: Assess the area of burn or large BSA rash.
- Access: Assess vascular access and the need for additional access catheters for the procedure.
- *Code Status/HCP*: What is the patient's code status? Who is the patient's health care proxy (HCP) and have they been informed and have they given consent for the anesthetic?

Intraoperative Management of the Severely Critically Ill Patient Should Focus on

- The timely identification and management of the most life threatening of the conditions
- Deployment of strategies to prevent worsening of the patient's condition while providing a chance to improve (to complete the much needed portion of the operation).
- Deployment of interventions to restore/replace vital organ function.
- Choice of Monitors and Access:
 - Physiologic monitors per standard of care
 - Consider invasive hemodynamic monitoring (arterial catheter; Swan-Gantz catheter vs. CVP monitoring), use of CO monitoring (Vigileo or others), TEE or transthoracic echo
 - Assess special need for monitoring bladder (abdominal compartment) pressure or ICP monitor
 - Secure large bore IV catheters (RIC line, Cordis in central vein, need for HD catheters, etc.)
- Airway Management: as discussed above.
- Ventilator Management:

- Use ARDSNet protective lung ventilation strategy for ARDS/ALI and septic patients.
- The use of inhaled prostacyclines may be necessary for lung injured patients with pulmonary hypertension.
- Use transport ventilators for patients with lung injury/contusion or at high risk for ALI/ARDS when in transit and ICU ventilators in the OR.
- Vasopressor Management: we will refer to other chapters for detailed discussion on the use of vasoactive agents (pressors).
- Transfusion Management: for discussion on transfusion goals and factor replacement for both actively bleeding patients and for patients who are NOT actively bleeding, please refer to Chapter 6.
- Fluid, electrolyte, and renal management:
 - For sepsis, see Chapter 10. For management of fluids and electrolytes, see Chapter 6.
 - Assess degree of renal injury (most often ATN in sepsis and hemorrhagic shock). Manage fluids to minimize further injury to the kidneys and to support recovery. When renal failure occurs acutely in the OR, instituting intraoperative renal replacement therapy maybe necessary (i.e., CVVH). Most common indications are intractable hyperkalemia, acidosis, and fluid overload leading to hypoxemia and heart failure.
- Pain management. Patients with chronic opioid use will require increased doses.
- Choice of Anesthetic Induction and Maintenance Agents:
 - Etomidate has minimal effect on blood pressure/CO, but may induce adrenal insufficiency. Propofol induction can be safe if dosed appropriately for the patient's hemodynamics (use reduced or incremental doses). Ketamine and opioid-based induction strategies can be used.
 - Severely critically ill patients may not tolerate intravenous or inhaled anesthetics, and may need to be managed with a high-dose opioid strategy.
- Choice of Muscle Relaxant Agents:
 - Many procedures maybe completed without muscle relaxation.
 - Because kidney injury is very common in severely critically ill patients, small doses of non-renally cleared muscle relaxants (cisatracurium or vecuronium) should be used as needed, titrated with the use of a nerve stimulator.
 - Early, short-term muscle relaxation may improve recovery from ARDS. However, consider the risk of critical illness myopathy and neuropathy.
- ACLS in the operating room: acutely life threatening conditions are managed in the OR according to ACLS (fatal arrhythmias) and ATLS (tension PTX, hemothorax, pericardial tamponade, hemorrhagic/hypovolemic shock) guidelines.
- Communication with ICU team and patient's family: continuity of care and the need for family involvement requires that all caretakers from the OR both document and communicate the course of events, the intervention they made and their outcomes to both the next care provider (nurses and physicians) in the ICU and the patient's family members.

EMERGENCY DEPARTMENT TO ICU COMMUNICATION STRATEGIES

PETER C. HOU, MD

KEY ELEMENTS OF INTEGRATED PRE- AND INTRAHOSPITAL CARE

- Protocolized care per current standards
- Multidisciplinary care, often by specialized care teams (trauma, cardiac arrest, STEMI, stroke, sepsis, etc.)
- Communication
 - Consider instituting a close-loop mechanism to prevent errors of omission
 - Institute appropriate, standardized hand-off processes
 - SBAR (Situation-Background-Assessment-Recommendation) technique (*Jt Comm J Qual Patient Saf.* 2006;32:167)
 - Describe patient situation and reason for admission
 - State pertinent history
 - Summarize facts and give your best current assessment
 - What tests are pending requiring follow-up, who has been consulted and what recommendations require follow-up, which therapies need to be continued and follow-up

CARE AND COMMUNICATION STRATEGIES FOR SPECIFIC DISEASE CONDITIONS

Trauma (Advanced Trauma Life Support, 8th Ed)

- Trauma team activation from EMS or ED emergency physician; traumatologist; neurosurgeon; orthopedic surgeon; emergency radiologist; interventional radiologist; intensivist; anesthesiologist; respiratory therapist; ED, interventional radiology (IR), operating room (OR), and all intensive care unit (ICU) personnel
- Hospitals designated as Level I Trauma Center (Level I TC)
 - Blood bank
 - Massive transfusion protocols
 - Protocols for administering reversal or adjunctive agents for hemorrhage (i.e., prothrombin complex concentrate, tranexamic acid)
- Hospitals not designated as Level I TC
 - Patients with multi-trauma, life threatening, or limb threatening injuries
 - Immediate transfer to a Level I TC (*J Trauma*. 2007;63:965)
 - Initial stabilize airway and breathing
 - No computed tomography should be performed
 - Plain films may be obtained without delaying patient transfer

• Facilitate transfer from ED \rightarrow TC, ED \rightarrow ICU, ED \rightarrow OR \rightarrow ICU, or ED \rightarrow IR \rightarrow ICU

Cardiac Arrest (Circulation. 2003;108:118; Circulation. 2008;118:2452)

- Activation of cardiac arrest team from EMS or ED emergency physician; intensivist; neurologist; ED and ICU personnel
- Continuous chest compressions (use automated chest compression devices if available)
- Consider activating cardiac catheterization laboratory (CCL) if electrocardiogram (ECG) shows ST-elevation or if high clinical suspicion for acute coronary syndrome
- Consider therapeutic hypothermia (TH) after return of spontaneous circulation (ROSC)
 - For ventricular fibrillation (level I evidence), pulseless ventricular tachycardia, and other non-perfusion rhythms
 - Review institutional inclusion of indications and contraindications
 - Avoid hyperoxia after ROSC (JAMA. 2010;303:2165)
- Initiate pre-hospital TH protocol if available by local EMS provider
- Transfer to institutions with TH protocol
- Facilitate coordinated transfer from ED \rightarrow ICU or ED \rightarrow CCL \rightarrow ICU

ST-Elevation Myocardial Infarction (STEMI) (Circulation. 2009;120:2271)

- STEMI team activation from the pre-hospital setting or ED emergency physician; interventional cardiologist; anesthesiologist; respiratory therapist; intensivist; ED, CCL, and ICU personnel
- ECG performed <10 min from presentation (pre-hospital ECG if available)
- Pre-hospital transfer to institution with percutaneous coronary intervention (PCI)
 - Goal door to balloon time: less than 90 min
- Pre-hospital transfer to institution without PCI
 - Consider transfer to PCI institution if there is no expected delay
 - Otherwise, consider thrombolysis (door to needle time: less than 30 min)
 - Consider transfer of patient after thrombolysis from ED to PCI institution
- Initiate other appropriate medical therapies
- Facilitate coordinated transfer from ED \rightarrow CCL \rightarrow ICU

Acute Stroke (Stroke. 2007;38:1633)

- Stroke team activation emergency physician; neurologist; emergency radiologist; interventional neuroradiologist; neurosurgeon; ED, IR, and ICU personnel
- Pre-hospital and ED stroke assessment National Institute of Health Stroke Scale
- Thrombolysis for symptom onset <3 hrs (Level I evidence)
 - Review contraindications to thrombolysis
- May consider thrombolysis for symptom onset up to 4.5 hrs
- Hospitals not designated as stroke centers (SC)
 - Facilitate transfer of patients to SC with or without thrombolysis
- Consider intra-arterial thrombolysis in selected patients
- Initiate other appropriate medical therapies
- Nothing by mouth until swallow evaluation to prevent aspiration
- Facilitate coordinated transfer from ED \rightarrow SC, ED \rightarrow ICU or ED \rightarrow IR \rightarrow ICU

Severe Sepsis & Septic Shock (CCM. 2008;36:296)

- Sepsis team activation emergency physician; intensivist; radiologist; interventional radiologist; surgeon; ED, IR, OR, and ICU personnel
- Pre-hospital sepsis screening with point of care lactate if available
- Consider instituting ED sepsis screening protocol for early identification
- Consider international guidelines for management of severe sepsis and septic shock
- Consider initiation of Early Goal-Directed Therapy (EGDT) protocol if local resources are available and feasible (*NEJM*. 2001;345:1368)
- Lactate clearance as goal for early septic shock therapy may be equivalent to EGDT and did not result in significantly different in-hospital mortality (*JAMA*. 2010;303:739)
- Early and appropriate antimicrobial therapy (administer antibiotics within the first hour)
- Facilitate coordinated transfer from ED \rightarrow ICU, ED \rightarrow IR \rightarrow ICU, or ED \rightarrow OR \rightarrow ICU

Acute Lung Injury (ALI) and Acute Respiratory Distress Syndrome (ARDS)

- Airway team activation emergency physician; anesthesiologist; respiratory therapist; intensivist; ED and ICU personnel (rapid response team if available)
- Prevent aspiration during endotracheal intubation (consider rapid sequence intubation)
- Consider low tidal volume (TV) ventilation (6–8 cc/kg) for patients with ALI (*ARDSNet, NEJM.* 2000;342:1301)
 - Use predicted body weight for tidal volume calculation
 - Maintain plateau pressure (Pplat) ≤30 cmH₂O
 - Apply appropriate fractional inspired oxygen and peak end-expiratory pressure
- Early identification of patients with risk factors to ALI development (AJRCCM. 2011;183:462)
 - Avoid high TV and Pplat to prevent ventilator-associated lung injury
- Avoid hyperoxia
- Facilitate coordinated transfer from ED → ICU

SUMMARY

- Care of the critically ill (CCM. 2007;35:1477)
 - Starts from pre-hospital setting and ED by way of CCL, IR, OR, into the ICU
- Must focus on:
 - Timely delivery of the standards of care for the specific disease condition
 - Improving the continuity of care between ED to the ICU
 - Facilitating patient transfer from EMS and ED (to sites of required resources and intervention) to the ICU
- Requires a coordinated multidisciplinary team approach
- Requires commitment from EMS, hospital, local, and regional resources

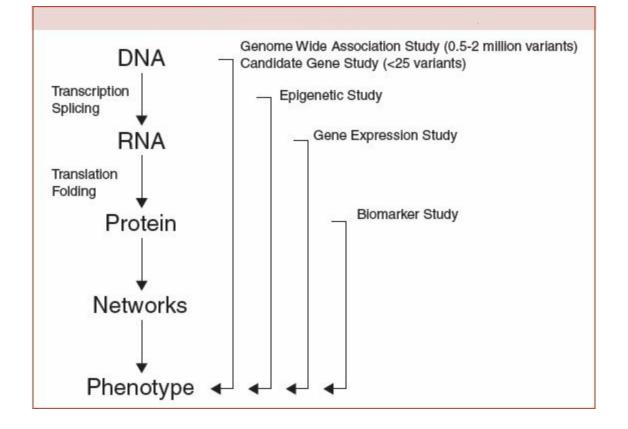
GENOMICS IN CRITICAL CARE

PEGGY S. LAI, MD • ANGELA J. ROGERS, MD, MPH

OVERVIEW

- The goal of a genomic study is to correlate certain genomic features of a patient with their phenotype
- Genomic features include:
 - DNA variation: single nucleotide polymorphism (SNP), copy number variation (CNV)
 - *Epigenetic markers*: heritable changes not related to the underlying DNA sequence; for example, histone modification, DNA methylation
 - Gene expression: variation in amount of transcribed messenger RNA (mRNA)
 - Biomarkers: variation in amount of translated proteins
- Phenotype is defined by certain patient characteristics, such as presence of shock
- Environmental exposures often interact with genomic features to produce the phenotype
 - Patients with a mutation in the *TLR4* gene (Asp299Gly) are more likely to develop septic shock in response to gram negative bacterial infection (*Arch Int Med.* 2002;162:1028)
- Penetrance is the proportion of subjects with a genetic variant that demonstrates the associated phenotype
 - Mendelian disorders such as Huntington's disease are associated with rare genetic variant(s) that have high penetrance
 - Complex diseases such as hypertension or acute respiratory distress syndrome (ARDS) are associated with common genetic variants with low penetrance, meaning that the presence of any single mutation increases the risk of disease only slightly

Figure 1. Genetic Features that Can Affect Phenotype



Unique Considerations When Performing Genomic Studies in Critical Care

- Most critically ill patients require a rare environmental exposure (trauma, severe infections) to develop disease, therefore precluding family-based studies
- Imprecise phenotype definitions decreases the signal to noise ratio (ex: ARDS may be common endpoint for many diseases), leading to a need for large sample sizes
- Many genetic studies in critical care use inappropriate control subjects (healthy subjects instead of at-risk subjects)
- Ethical issues with genotyping, as the patient often cannot give consent
- Timing of when to measure genomic features is key in gene expression and biomarker studies, as RNA and protein levels may vary greatly during patient's clinical course

CANDIDATE GENE AND GENOME WIDE ASSOCIATION STUDIES (GWAS)

- Goal: Genetic variation in the form of SNPs are compared in cases and controls using large groups of unrelated subjects or case and control families
 - SNPs are individual base changes in DNA, many of which are common in the population. Most SNPs in these studies are of unknown function
 - Linkage disequilibrium (LD) refers to different genetic variants that track together in a specific population. This can make it difficult to determine if a SNP associated with disease is a causal variant or simply a marker that is in LD with the disease-causing SNP
 - A haplotype refers to two or more SNPs that are in linkage disequilibrium and, therefore, always inherited together

- While candidate gene studies evaluate small numbers (<25) of pre-selected genetic variants, GWAS evaluate large numbers (>0.5 million) of variants to discover genes important in disease
- Susceptibility to many disorders seen in critical care such as risk of death from infection appear to have genetic components (*PLOS One.* 2010; 5(5):e10603), supporting the use of these studies in this setting

CURRENT USE OF GENOMICS IN CRITICAL CARE

- Currently, there is no established role for genetic testing in the ICU setting in adults. However, several areas appear particularly promising, and may soon have applications
- Candidate Gene Studies:
 - SNPs have been associated with sepsis outcome in multiple biologic pathways such as the toll-like receptor pathways, inflammatory and anti-inflammatory mediators (TNF- α , IL-6), and coagulation pathways
 - Candidate gene studies with direct clinical implications include the association between β adrenergic receptor gene polymorphisms and increased mortality in septic shock; this deleterious genotypic effect was eliminated in patients treated with low-dose corticosteroids (*Am J Respir Crit Care Med.* 2010;181:143)
- Biomarkers:
 - Peptidase inhibitor 3 is a neutrophil elastase inhibitor that has been identified as a biomarker in ARDS (*Am J Respir Crit Care Med.* 2008;38:724)
 - Procalcitonin, a biomarker for severe bacterial infection in patients with suspected sepsis, has been used to reduce the duration of antibiotic use from 14.3 to 11.6 days in the PRORATA trial (*Lancet*. 2010; 375:463) although further clinical studies needed
- Pharmacogenetics:
 - Mutations in several enzymes involved in drug metabolism show promise in clinical care, though they have not been specifically assessed in ICU patients
 - Two particularly compelling examples include *VKORC1* in warfarin dosing (*NEJM*. 2008; 358(10):999) and reduced *CYP2C19* function and increased cardiovascular events while taking clopidogrel (*NEJM*. 2009;360(4):354). Large randomized clinical trials that test whether altered dosing of these medications based on genotype changes outcome are underway
 - Polymorphisms in *SLCO1B1* are associated with the development of statin-induced myopathy (*NEJM*. 2008;359(8):789), which has future implications for possible therapeutic use of this class of medications for sepsis and ARDS in the ICU

FUTURE APPLICATIONS

• Our understanding of the human genome has exploded in the 10 yr since the first copy of the Human Genome sequence was published. Applications of these advances to the routine care of patients with complex diseases (non-Mendelian) are close at hand. Knowing, for example, that a patient contains certain high-risk SNPs, one could choose one vasopressor over the other, start with a higher dose of a warfarin, and avoid a class of antipsychotics because of the risk of long-QT is simply too high for these patients

ICU CALCULATORS, CALCULATIONS, DRUGS

SUJATHA PENTAKOTA, MD

HEMODYNAMIC FORMULAS

Variable	Calculation	Normal	
Cardiac index(CI)	CO/BSA	2.5-4.0 I/min	
Stroke volume	CO × 1,000/HR	60-90 ml/beat	
MAP	DBP + PP/3	60-110 mm Hg	
SVR	MAP-CVP × 80	800–1,500 dynes × sec/cn	
PVR	PAP-PAOP × 80	150–250 dynes × sec/cm ⁵	
LVSW	$SV \times (MAP-PAWP) \times 0.0136$	58-104 gm-m/beat	
RVSW	$SV \times (MPAP-PAWP) \times 0.0136$	8-16 gm-m/beat	
CO	HR × SV	5–8 I/min	
Corrected QT (QTo	c) = Bazett's formula = QT interval/ $$	RR interval)	

Fick Cardiac Output

- Oxygen consumption $(1/min) = CO(1/min) \times arteriovenous$ (AV) oxygen difference
- CO = oxygen consumption/AV oxygen difference
- Oxygen consumption must be measured (can estimate w/ 125 ml/min/m², but inaccurate)
- AV oxygen difference = Hb (g/dl) \times 10 (dl/l) \times 1.36 (ml O_2/g of Hb) \times (Sa O_2 Sv O_2)
 - SaO₂ is measured in any arterial sample (usually 93%–98%)
 - SvO_2 (mixed venous O_2) is meaured in RA, RV, or PA (assuming no shunt) (normal ~75%)

$$\therefore \textbf{Cardiac output (I/min)} = \frac{Oxygen \ consumption}{Hb \ (g/dI) \times 13.6 \times (SaO_2 - SvO_2)}$$

RESPIRATORY FORMULAS

Variable Formula		Normal Value		
Alveolar oxygen Tension	$PAO_2 = (FiO_2 \times (P_{atmos} - PH_2O)) - (PaCO_2/RQ)$	110 mm Hg on FiO ₂ 0.21		
Alveolar-arterial oxygen gradient	A-a gradient = PAO ₂ - PaO ₂	10 mm Hg at FiO ₂ 0.21. Increases 5–7 mm Hg per 10% increase in FiO ₂ . At FiO ₂ 1.0, should be <150 mm Hg		
Oxygen extraction ratio	$OER = VO_2/DO_2 \times 100$ $(CaO_2 - CvO_2)/CaO_2) \times 100$	22%–32%		
Partial pressure of	Pacco VVCO2	35-45 mm Hg		
arterial carbon dioxide	$PaCO_2 = K \times \frac{VCO_2}{(1 - V_d/V_t) \times VA}$			
Arterial oxygen content	$CaO_2 = (SaO_2 \times Hb \times 1.34) + 0.003 (PaO_2)$	17-20 ml/dl		
Mixed venous oxygen content	$SvO_2 = SaO_2 - (VO_2/Q \times Hb \times 13)$	12–15 ml/dl		
Intrapulmonary shunt	$Qs/Qt = (CcO_2 - CaO_2)/$ $(CcO_2 - CvO_2)$	5%		
Physiologic dead space	$V_d/V_t = PaCO_2 - PeCO_2/PaCO_2$	Negligible		
Oxygen consumption	$VO_2 = Q \times [(CaO_2 - CvO_2)]$	200-250 ml/min		
Delivered oxygen	$DO_2 = Q \times CaO_2$	520-570 ml/min/m ²		
Static compliance	TV/Plateau pressure - PEEP	0.05-0.07 I/cm H ₂ O		
Dynamic compliance	TV/PIP – PEEP	80-100 ml/cm H ₂ O		
Airway resistance	PIP – Plateau pressure peak inspiratory flow	4–6 cm H ₂ O·l ^{−1} ·sec ^{−2}		

PAO₂, partial pressure of alveolar oxygen; FiO₂, fraction of inspired oxygen; P_{atmos} , barometric pressure (760 mm Hg at sea level); PH_2O , water vapor pressure; RQ, respiratory quotient; $PaCO_2$, partial pressure of carbon dioxide in blood; K, constant; $VCO_{@}$, carbon dioxide production; V_d/V_t , dead space ratio of each tidal volume breath; VA, min ventilation.

ACID-BASE EQUATIONS (ALSO SEE CHAPTER 7)

Base deficit (mEq/l) = $0.5 \times \text{body weight in kg} \times [24 - (HCO_3)]$

Anion gap = $(Na^+ + K^+)$ - $(Cl^- + HCO_3)$. Normal AG = 3 - 12 mEq/l.

Delta gap = Anion gap - 12 (normal anion gap)

Corrected anion gap: AG needs to be corrected for albumin level. For every 1 g/dl decrease in albumin from 4 g/dl, AG decreases by 2.5.

DELTA GAP

$$\Delta$$
 gap = (AG-12) - (24-HCO₃) = 0 ± 6

Delta ratio =
$$\Delta$$
 anion gap/ Δ [HCO₃-] = $\frac{AG-12}{24-HCO_3}$

Positive delta gap signifies a concomitant metabolic alkalosis or respiratory acidosis.

Negative delta gap signifies a concomitant normal anion gap metabolic acidosis or chronic respiratory alkalosis.

RENAL

Calculated osmolarity = 2 (Na⁺) +
$$\frac{BUN (mg/dl)}{2.8}$$
 + $\frac{Glucose (mg/dl)}{18}$ + $\frac{Ethanol}{4.6}$

Normal serum osmolarity = 285–295 mOsm/l

Osmolar gap = measured osmolarity – calculated osmolarity (normal <10)

Fractional excretion of sodium:

FENA: Urine Na \times serum Cr/(urine Cr \times serum Na) \times 100

FENA < 1: Prerenal

It may also be seen in patients with post-ischemic ATN, ATN superimposed upon a chronic prerenal disease, in 10% of patients with nonoliguric ATN, in AKI due to radio contrast media or heme pigments, acute glomerulonephritis or vasculitis, hepatorenal syndrome and in some cases of acute interstitial nephritis, and (rarely) acute urinary tract obstruction.

FENA = 1–2: Prerenal or Renal FENA > 2: ATN

Results not reliable in patients on diuretics. Hence in patients on diuretics, consider using:

Fractional excretion of urea: <35 in prerenal disease, >50 in ATN.

Fractional excretion of lithium: <15% (and usually below 10%) in prerenal disease.

Fractional excretion of uric acid: <12 in prerenal disease, >20 in ATN.

Estimation of GFR

- Serum creatinine concentration
- Creatinine clearance
- Estimation equations based upon the serum creatinine: such as the Cockcroft–Gault equation and modification of diet in renal disease (MDRD) study equations

Creatinine Clearance

Creatinine clearance (CrCl) =
$$\frac{\text{Urine Creat (mg/dl)} \times \text{Total urine output in 24 hrs (ml/d)}}{\text{Serum Creat (mg/dl)} \times 1,440}$$

This gives CrCl in ml/min. This may be adjusted for the BSA using the formula:

 $CCr \times 1.73/BSA$ to give CrCl in terms of ml/min/1.73 m².

The normal value for the creatinine clearance is 95 ± 20 ml/min in women and 120 ± 25 ml/min in men

Two major errors can limit the accuracy of creatinine clearance

- Incomplete urine collection
- Increasing creatinine secretion as the GFR falls
- Cockcroft–Gault equation

$$CCr (ml/min) = \frac{(140 - Age) \times lean body weight (kg)}{Cr [mg/dl] \times 72}$$

In women, multiply by 0.85. This equation has to be adjusted for body surface area.

MDRD GFR calculator

The MDRD study equation is reasonably accurate in non-hospitalized patients known to have CKD, regardless of diagnosis.

The MDRD study equation and Cockcroft–Gault equation appear to be somewhat less accurate in obese individuals.

The MDRD study equation and Cockcroft–Gault equation may not be similarly accurate in different age groups.

The MDRD study and the Cockcroft–Gault equations are less accurate in populations with normal or near normal GFR.

Estimation equations may also be less accurate in populations of different ethnicities and from outside of the United States.

ICU MEDICATIONS AND DOSES

Cardiac Meds

Norepinephrine	0.02-3 mcg/kg/min	Tachycardia, arrhythmias
Epinephrine	0.01-0.1 mcg/kg/min	Tachyarrhythmias
Vasopressin	0.1–0.4 units/min	Arrhythmias, asystole, decreased CO, mesenteric ischemia
Phenylephrine	0.3 mcg/kg/min. Max 3 mcg/kg/min	Decreased CO, hypersensitivity reactions
Dopamine	1–2 mcg/kg/min. Max 15 mcg/ kg/min	Ectopic beats, tachycardia, angina pain, headache, nausea, vomiting
Dobutamine	1–2 mcg/kg/min. Max 10 mcg/ kg/min	PVC, tachycardia, hypo/hypertension
Milrinone	Bolus 50 mcg/kg 0.1-0.75 mcg/kg/min	PVC, NSVT, hypotension, headache

PULMONARY VASODILATORS

Calcium channel blockers	Up to 720 mg/d	Edemas, headache, AVN block, dizziness
Diltiazem Nifedipine	Up to 240 mg/d	Flushing, peripheral edema, dizziness, headache, nausea, dyspepsia
Prostacyclins Epoprostenol Trepostinil Iloprost	25–40 ng/kg/min IV 50–100 ng/kg/min 2.5 mcg–5 mcg inhaled	Flushing, jaw pain, and diarrhea Flushing, cough
Endothelin antagonists Bosentan	Oral: 62.5 mg q12h × 4 wks Max 125 mg q12	Edema, headache, inhibition of spermatogenesis, anemia, increase in transaminases
PDE-5 inhibitors Sildenafil	IV: 10 mg q8h PO: 20 mg TID	Headache, flushing, diarrhea, myalgia, dyspepsia, erythema
Nitric oxide	20–40 ppm inhaled	Hypotension, withdrawal syndrome, hypoxemia, pulmonary edema

DRUGS USED IN HYPERTENSIVE EMERGENCIES

Nitroprusside	0.25–3 mcg/kg/min Max 10 mcg/kg/min	Onset: few seconds Duration: 2–3 min after infusion stopped	Nausea, vomiting, hypoten- sion, tachycardia, thiocya- nate, cyanide toxicity
Nitroglycerin	5-20 mcg/min. Max 40-400 mcg/min	Onset: 5–10 min Duration: 5–15 min after infusion stopped	Hypotension, tachycardia, headache
Nicardipine	3–15 mg/hr	Onset: 15–30 min Duration: 1–4 hrs	Hypotension, tachycardia, headache, peripheral edema
Labetalol	IV bolus – 20–40 mg (max 80 mg) at 10–20 min intervals. Infusion 0.5–2 mg/min	Onset: 5–10 min Duration: 3–6 hrs	Hypotension, bradycardia, heart block, bronchocon- striction
Hydralazine	10-40 mg q4-6h	Onset: 2–4 hrs 10–30 min Duration:	Hypotension, tachycardia, headache. Drug-induced lupus like syndrome, rash, peripheral neuropathy
Enalaprilat	1.25–5 mg IV q6h	Onset: 15–30 min Duration: 6–12 hrs	Hypotension, hyperkalemia, renal insufficiency, anaphy- laxis, angioedema
Clonidine	0.1–0.3 mg PO q8–12h	Onset	Drowsiness, dizziness, hypotension, bradycardia, dry mouth
Esmolol	Bolus – 500 mcg/kg Infusion: 50–100 mcg/kg/min	Onset: 1–5 min Duration: 15–30 min	Bradycardia, hypotension, bronchospasm
Phentolamine	Bolus: 5–10 mg Infusion: 0.2–5 mg/min	Onset: 1–2 min Duration: 10–20 min	Tachycardia, nausea, headache

Anti-arrhythmic Agents

Class	Electrocardiographic Effect	Membrane Effect	Example
IA	↑ QRS & ↑ Q-T interval	Sodium channel block	Quinidine Procainamide Disopyramide
IB	↓ Q-T interval	P-T interval Sodium channel block	
IC	↑↑ QRS interval	Sodium channel block	Flecainide Propafenone Moricizine
II	↓ HR; ↑ P–R interval	β-adrenergic receptor inhibition	Propranolol and others
III	↑ Q-T interval	Potassium channel block; slow sodium channel facilitator	Procainamide Sotalol Amiodarone Ibutilide
IV	↓ HR; ↑ P-R interval	Calcium channel block	Verapamil Diltiazem
Digitalis	↑ P-R interval; ↓ Q-T interval	Na+, K+ ATPase inhibition	Digoxin
Adenosine	↓ HR; ↑ P–R interval	Purinergic receptor agonist	Adenosine

Drug	Dose	Common Toxicities	Rare Toxicities
Quinidine	324-648 mg q8h	Diarrhea, thrombocy- topenia, TDP (2%–8%)	Hepatitis, bone marrow depression, cinchonism
Procainamide	15–18 mg/kg bolus, then 1–6 mg/min	Hypotension, slowing of conduction, diarrhea, nausea, vomiting	Torsades de pointes, drug-induced lupus syndrome
Disopyramide	100-200 mg 6 hrs 200-400 mg q12h	Precipitation of glau- coma, constipation, dry mouth, urinary retention, TDP	
Lidocaine	1–1.5 mg/kg bolus, then 1–4 mg/min		Confusion, slurred speech, drowsiness, paresthesias, seizures, bradycardia
Flecainide	50-200 mg q12h	Blurred vision, provo- cation or exacerba- tion of potentially lethal arrhythmias	Heart block
Propafenone	150–300 mg q8h	Re-entrant ventricular tachycardia, exacerba- tion of heart failure, sinus bradycardia, bronchospasm	
Propranolol	Load: 1–3 mg IV, the 10–80 mg PO q6–8h	Bradycardia, hypoten- sion, CHF, broncho- spasm	
Sotalol	80-320 mg q12h	TDP	
Amiodarone	300 mg bolus, then 1 mg/min for 6 hrs, then 0.5 mg/min for ≥18 hrs	Bradycardia, hypoten- sion, nausea	Heart block, pulmonary fibrosis, hypo/hyper thyroidism, corneal micro deposits, blue-gray discoloration of skin, optic neuropathy, Torsades de pointes
lbutilide	1 mg IV over 10 min, may repeat once 10 min later	TDP in 6%	•
Verapamil	5 mg/kg bolus, then 5–15 mg/hr	Headache, flushing, edema	
Diltiazem	0.25 mg/kg bolus, then 5-15 mg/hr	Bradycardia, hypoten- sion, constipation	Heart block, heart failure
Digoxin	Loading: 5–15 mcg/ kg; give 50% of load in initial dose, then 25% at 6–12 hrs intervals × 2	Nausea, vomiting, PVCs, bigeminy, tri- geminy, ventricular tachycardia, ventricular fibrillation, PAT, nodal rhythms, accelerated junctional tachycardia and sinus bradycardia, AV conduction block	
Adenosine	6 mg IV, if not effec- tive in 1–2 min can give 12 mg, may repeat 12 mg	Transient asystole, chest fullness and dyspnea	Bronchospasm, atrial fibrillation

RELATIVE POTENCIES AND EQUIVALENT DOSES OF REPRESENTATIVE CORTICOSTEROIDS

Steroid	Glucocorticoid (Anti- inflammatory)	Mineralocorticoid (Sodium Retention)	Half-life (hrs)	Equivalent Dose
Cortisol	1	1	8-12	20
Cortisone	0.8	0.8	8-12	25
Fludrocortisone	10	125	12-36	NA
Prednisone	4	0.8	12-36	5
Prednisolone	4	0.8	12-36	5
Methylprednisolone	5	0.5	12-36	4
Triamcinolone	5	0	12-36	4
Betamethasone	25	0	36-72	0.75
Dexamethasone	25	0	36-72	0.75

ANTICOAGULANTS

Drug	Dosage	Half- life	Monitoring	Elimination	Use in	Antidote
Unfractionated heparin	The state of the s		aPTT 1.5–2.5 × control	Renal	HIT NO	Protamine
Low molecu- lar weight Heparin Enoxaparin (Lovenox) Tinzaparin (Innohep) Dalteparin (Fragmin)	1 mg/kg SubQ q12h/ 1.5 mg/kg SubQ q24h 175 U/kh SubQ q24h 120 U/kg SubQ q12h	4.5–7 hrs 3–5 hrs 2–5 hrs		Renal	NO	Partial reversal with prot- amine
Direct Thrombin inhibitor Argatroban	0.5–2 mcg/kg/ min-titrated to aPTT of 1.5–3 times control. Max 10 mcg/kg/ min PCI: 350 mcg/kg bolus, 25 mcg/ kg/min HIT: 2 mcg/kg/min (adjustments made as clinically indicated, not to exceed 10 mcg/ kg/min) *ICU, HF, MOSF, severe anasarca, after cardiac sur- gery: 0.5–1.2 mcg/ kg/min	40–50 min	aPTT q4h until steady state reached (1.5–2 times baseline), ACT	Hepatic	YES	NO
Fondaparinux (Arixtra) Indirect factor Xa inhibitor	DVT prophylaxis: >50 kg: 2.5 mg qd SubQ Acute DVT/PE treatment: SubQ <50 kg: 5 mg qd 50–100 kg: 7.5 mg qd >100 kg: 10 mg qd	17–21 hrs	Anti-Xa activity of fondaparinux can be measured by the assay if fondaparinux is used as the calibrator	77% excreted unchanged in urine. T1/2: 17–21 hrs	YES Unlabelled use	NO
Bivalirudin Semisynthetic hirulog	PCI: 0.75 mg/kg bolus, followed by 1.75 mg/kg/h during and up to 4 hrs post- procedure. HIT (unlabeled use): IV: normal renal function: ini- tial dose: 0.15–0.2 mg/kg/hr; adjust to aPTT 1.5–2.5 times baseline value	25 min	aPTT every 4 hrs until steady state reached (1.5–2 times baseline), ACT	80% enzymatic 20% renal	, YES	NO

Lepirudin DTI	HIT: omit bolus or \$\frac{1}{2}\$ 0.2 mg/kg in life or limb threatening thrombosis, followed by 0.10 mg/kg/hr *ICU: No bolus, 0.005–0.10 mg/kg/hr Hemofiltration: 0.005–0.01 mg/kg/hr, no bolus Dialysis: 0.1 mg/kg bolus pre-dialysis PCI: not indicated	80 min	aPTT every 4 hrs until steady state reached (1.5–2 times baseline)	Renal	YES	NO
Danaparoid Factor Xa inhibitor (Organon)	HIT: Bolus-IV 2,000 anti-factor Xa units Then, 2,000 units subQ q12h	25 ± 100 hrs	Anti-factor Xa assay	Renal	YES	NO
Coumadin	2–5 mg PO qd	40 hrs (20–60 hrs)	INR	Hepatic metabolism, renal excretion	NO	Vitamin K FFP ?FVIIa ?FIX complex

New Anticoagulants

Drug	Target	Route	Dose (VTE Pre- vention)	Half- life	Monitoring Required	Excretion	Antidote
Rivaroxaban	Direct factor Xa inhibitor	PO	10-40 mg qd	7–11 hrs	none	Renal 66% Hepatic 33%	None
Apixaban	Direct factor Xa inhibitor	PO	2.5 mg PO q12h	8–14 hrs	FXa inhibition assay or modified PT	Renal 25%	None
Dabigatran (DTI)	Factor IIa	РО	220 mg qd	14–17 hrs		Renal >80%	None
Otamixaban	Direct factor Xa inhibitor	IV		30 min	none	Biliary 75%	None

PHARMACOLOGIC COUMADIN REVERSAL

Vitamin K (phytonadione)	1-10 mg q24h - subQ/PO/IV	IV form-anaphylaxis, hypotension
Activated factor 7	15-90 mcg/kg	Thrombosis, hypertension
Factor IX complex	INR 2-3.9: 25 U/kg INR 4-5.9: 35 U/kg INR > 6: 6 U/kg	Thrombosis, DIC

Insulin Preparations

Туре	Action (hrs) Onset	Peak	Duration
Rapid			
Regular crystalline	0.5-0.7	1.5-4	5–8
Lispro	0.25	0.5-1.5	2–5
Aspart	0.25	0.6-0.8	3–5
Glulisine	-	0.5-1.5	1-2.5
Intermediate			
NPH	1–2	6-12	18-24
Lente	1–2	6–12	18-24
Slow			
Ultralente	4-6	16-18	20-36
Protamine zinc	4-6	14-20	24–36
Glargine	2–5	5-24	18–24

DIURETICS

Drug	Mechanism and Site of Action	Dose	DOA	Common Adverse Effects
Acetazolamide	Inhibitor of carbonic anhy- drase — increases excretion of bicarb Site: PCT	125–500 mg IV/ max of 2 g PO	IV 4–5 hrs PO 8–12 hrs	Hypokalemia Aplastic anemia Hyperglycemia Thrombocytopenia Hypersensitivity in sulfa allergy patients
Mannitol	Osmotic diuretic Site: PCT	0.25–1 g/kg	1.5–6 hrs	CHF, hyper/hypoten- sion, fluid and electro- lyte imbalance
Furosemide	Inhibitors of Na-K-2CI symport Site: thick AL of LOH	10-40 mg IV	6 hrs	Electrolyte imbalance Dehydration Deafness Hyperglycemia Hyperuricemia Hypersensitive reaction in sulfa allergy patients
Bumetanide	Inhibitors of Na-K-2CI symport Site: thick AL of LOH	0.5-1 mg IV. Max 10 mg/d	2-4 hrs	Electrolyte imbalance Dehydration Deafness Hypersensitivity in sulfa allergy
Ethacrynic acid	Inhibitors of Na-K-2CI symport Site: thick AL of LOH	IV: 25–100 mg over 5–10 min. Max 400 mg/d Oral: 50–200 mg/24 hrs	IV – 2 hrs Oral: 12 hrs	Can be used in patients with sulfa allergy
Torsemide	Inhibitors of Na-K-2CI symport Site: thick AL of LOH	PO/IV: 20 mg qd, max 200 mg/d Infusion: 5–20 mg/hr	PO 6–8 hrs	EKG abnormality, chest pain, nervousness
Chlorothiazide (DIURIL)	Inhibitor of Na-Cl symport Site: DCT	250–500 mg IV, max 2 g over 24 hrs	Oral: 6–12 hrs IV – 2 hrs	Enhances activity of loop diuretics in renal failure
Chlorothiazide	Inhibitor of Na-Cl symport Site: DCT	50–100 mg PO qd. Max 200 mg/d	Oral: 2–6 hrs	Cardiac dysrhythmia Cholestatic jaundice syndrome, pancreatitis pulmonary edema Toxic epidermal necrolysis

SEDATIVES (ALSO SEE CHAPTER 8)

Drug	Route	Bolus	Infusion	Adverse Effects
Benzodiazepines Midazolam	IV	1 mg repeated	0.04-0.2 mg/	CNS depression, respiratory depression, paradoxical excitation
i ildazolalii	1.4	to effect	kg/hr	
Diazepam	IV	2–5 mg IV push q1–4h	ŇA	
Lorazepam	IV, IM	1-4 mg q4-6h	0.01–0.05 mg/ kg/hr	
Propofol	IV	0.3-0.7 mg IV push	10–100 g/kg/ min	Hypotension, bradycardia, hypertriglyceridemia
Dexmedetomidine	IV	10 mcg/kg	0.2-0.7 g/kg/hr	Hypotension/hypertension, bradycardia
Ketamine	IV	1–2 mg/kg IV push	0.5-4.5 g/kg/hr	Hallucinations, tachycardia
Barbiturates Pentobarbital Thiopental	IV IV	3–5 mg/kg 3–5 mg/kg	1–3 mg/kg/hr 2–5 mg/kg/hr	Hypotension, tachycardia, respiratory depression
Butyrophenones Haldol	IV, IM	0.5–5 mg, repeat doses every 30–45 min. Max 80 mg PO/IV q6h		CNS depression, orthostatic hypotension, QTc prolongation, extrapy- ramidal side effects, neuro- leptic malignant syndrome

IM, intramuscular; IV, intravascular; NA, not applicable

DOSAGE AND MODE OF ADMINISTRATION OF COMMON NONOPIOID ANALGESICS

Drug	Route	Dose (mg)	Frequency
lbuprofen	PO	200-400	q4-6h
Ketorolac	IM	30-60 initially	Repeat 15-30 q4-6h
Indomethacin (Indocin)	PO, PR	25 (PO), 50 (PR)	q6-8h
Naproxen (Naprosyn)	PO	250-500	q12h
Acetaminophen	PO, PR	500-1,000	q4-6h
Aspirin	PO, PR	300-1,000	q4-6h

STANDARD EQUIVALENTS OF SELECTED OPIOID ANALGESICS

Drug	Oral Dose (mg)	Parenteral Dose (mg)
Alphaprodine HCl (Nisentil)	-	45
Codeine	200	130
Fentanyl (Sublimaze)	_	0.1
Hydromorphone HCI (Dilaudid)	7.5	1.5
Meperidine HCI (Demerol)	200	50
Methadone HCI (Dolophine HCI)	10	8.8
Morphine sulfate	60	10
Oxycodone HCI (Roxicodone)	30	15
Oxymorphone HCI (Numorphan)		1.5
Pentazocine (Talwin)	_	60

Acceptable Drugs, Intravenous Drugs, and Lockout Intervals for Use with Postoperative Patient-controlled Analgesia Pump

Drug	Dose (mg)	Lockout Interval (min)
Morphine sulfate	0.2-3	5–20
Meperidine HCI (Demerol)	2-30	5–15
Fentanyl (Sublimaze)	0.02-0.1	3–10
Hydromorphone HCl (Dilaudid)	0.02-0.5	5–15

Miscellaneous

	Indications	Dosage	Excretion	Side Effects
Acetylcysteine	Acetaminophen overdose Prophylaxis for contrast-induced nephropathy	In acetaminophen overdose Oral: 140 mg/kg × 1 dose, 70 mg/kg every 4 hrs × 17 doses IV: 150 mg/kg × 1 dose, 50 mg/kg × 2 dose over 4 hrs, 100 mg/kg × 1 dose over 16 hrs	Excreted by kidneys	IV: anaphylactoid reactions, flush- ing, tachycardia, urticaria, nausea, vomiting
Adenosine	PSVT, WPW syndrome	6-12 mg IV bolus	Cleared by RBCs and endothelial cells	Transient new arrhythmia, facial flushing, headache, dizziness, chest pressure, dyspnea
Alprostadil (PGE1)	PHTN, maintain patent ductus arteriosus	0.05–0.1 mcg/ kg/min	Pulmonary metabo- lism/renal excretion	IV: flushing, fever, apnea
Alteplase (recombinant tPA)	Fibrinolytic agent— lyse fibrin in thrombus in coronary artery, pulmonary artery, cerebral artery; used for central venous catheter clearance	Wt > 67 kg 15 mg bolus and then 15 mg over 30 min. Institute heparin therapy and then infuse 35 mg of TPA over 1 hr. Total dose of tPA – 100 mg Wt < 67 kg – 5 mg bolus, then 0.75 mg/kg over 30 min, heparin bolus and then 0.5 mg/kg tPA over 1 hr	Hepatic clearance	Hemorrhage, fever
Aminocaproic acid	Antifibrinolytic agent	Load: 5 g over 1 hr. Maintenance 6-24 g/24 hrs. Max 24 hr dose: 30 g	Renal	Arrhythmias, bradycardia, edema, throm- bosis, confusion, rash, agranulocy- tosis
Tranexamic acid	Antifibrinolytic agent	In trauma – associated hemorrhage: IV: load 1,000 mg over 10 min, followed by 1,000 mg over next 8 hrs	Renal	Hypotension, diarrhea, nausea, vomiting, blurred vision

Naloxone	IV 0.4–2 mg, may repeat every 2–3 min. Consider repeating the dose q20–60 min depending on type/duration of opioid/starting an infusion. For infusion, use 2/3 of the initial effective naloxone bolus	30–120 min	Hepatic	Tachycardia, hypertension, pain, agitation (secondary to reversal of opi- oid and sedative effect), pulmo- nary edema
Flumazenil	Reversal of ben- zodiazepine effect	0.01 mg/kg up to 0.2 mg, repeat up to 1 mg	Hepatic	Agitation, seizures

STATISTICS AND EVIDENCE-BASED MEDICINE (EBM)

SUJATHA PENTAKOTA, MD

EVALUATION OF PUBLISHED RESEARCH

Apply the following questions to the manuscript:

Are the results valid?

Was the assignment of patients to treatments randomized?

Were all patients who entered the trial properly accounted for and attributed at its conclusion?

Was follow-up complete?

Were the patients analyzed in the groups to which they were randomized?

Were the patients, health workers, and study personnel blind to treatment?

Were the groups similar at the start of the trial?

Aside from the experimental intervention, were the groups treated equally?

What are the results?

How large was the treatment effect?

How precise was the estimate of the treatment effect?

Will the results help me in caring for my patient?

Can the results be applied to my patient care?

EBM Internet Sources

- Cochrane database of systematic reviews: www.cochrane.org
- Additional resources: www.cebm.net; www.openclinical.org; ktclearinghouse.ca/CEBM
- Medline: www.pubmed.org

Definitions:

- Odds and odds ratios: odds are the probability of an event occurring divided by the probability of the event not occurring.
- An odds ratio is the odds of the event in one group, for example, those exposed to a drug, divided by the odds in another group not exposed.
- **Relative risk:** the relative risk is the ratio of the probabilities of two events; if p is the probability of the first event, and q is the probability of the second, then the relative risk is p/q.

A Basic Guide for Systematically Evaluating and Applying Evidence-Medicine

Study	A Basic Guide fo	What are the		падр	Jying Lyidence-	Will the Results Help Me in My Patient Care
Diagnostic	Was there an independent, blind comparison with a reference (gold) standard of diagnosis? Was the diagnostic test evaluated in an appropriate spectrum of patients, similar to the practice population?	A diagnostic tes specificity. Positi	st is validated by ive and negative	predicti		a. Is the test available, affordable, accurate and precise in your setting? b. Estimate your patient's pretest probability? c. Will the post-test probability affect your management
	Was the reference standard applied regardless of the diagnostic test result?	Diagnostic Target Disorder Test Result Present Absent Totals		Totals	plan and benefit the patient?	
	A diagnostic test is validated by its degree of sensi- tivity, specificity. Positive and negative predictive values.	Positive Negative	a b		a + b c + d	
	values.	Totals	d a + c b + d		a + b + c + d	
		Sensitivity = a/a + c Specificity = d/b + d Likelihood ratio (LR) of a positive test = sens/1-spec Likelihood ratio of a negative test = 1-sens/spec Positive predictive value = a/a + b Negative predictive value = d/c + d Prevalence of a disease = a + c/a + b + c + d Pre-test odds ratio = prevalence/1-prevalence Post-test odds = pretest odds × LR			= 1-sens/spec	
Prognosis	Was a defined, representative sample of patients assembled at a common point in their disease course? Was patient follow-up sufficiently long and complete? Were objective outcome criteria applied in a "blind" fashion? In subgroups with different prognosis, was there an adjustment made for important prognostic factors and was there validation in an independent group of 'test set' patients?				tudy population ? s of the likeli-	Are the study patients similar to your patient group? Will the results significantly impact your conclusions as to what to offer or tell your patients?
Treatment and RCT	Was the assignment of patients to treatment randomized? Was the randomization concealed? Were all the patients who entered the trail accounted for at conclusion? Were the patients analyzed the groups to which they were randomized? Were the patients and clinicians blinded to treatment? Were the groups treated equally except for the	Relative risk reduction (RRR) RRR = control event rate — experimental event rate/ control event rate Absolute risk reduction (ARR): control event rate — experimental event rate. Number of patients needed to treat to prevent one bad outcome (NNT): 1/ARR.				Were all the clinically important strategies and outcomes included? Are the probabilities credible? Was the robustness of the conclusion tested?
Systematic review	were the groups treated equally except for the experimental treatment? Were the groups similar at the start of the trial? Is it an overview of randomized trials of treatment you are interested in? Does it include a methods section that describes: finding and including all relevant trials? Assessing their individual validity? Were the results consistent from study to study?	How large and precise are the results? This may be concurred from the 95% confidence interval.			onfidence	Are the study patients similar to my patient population? Were all clinically important outcomes considered? Cost-benefit analysis – does benefit outweigh harm and costs?
Economic analysis	Is this report asking an economic question comparing well-defined alternative courses of action with a specified point of view from which the costs and effects are being viewed? Does it cite good evidence of the efficacy of the alternatives? Does it identify all the costs and effects you think should and did it select credible measures for them?	Two-step process: 1. Are the resulting costs or costs/unit of health gained impressive? 2. Could the uncertainty in the evidence change the results? Check if the study includes a cost-effectiveness analysis/cost-benefit analysis/cost-utility analysis.			e change the	Could my patients expect similar health outcomes and costs? Are the benefits worth the harm and costs?
Clinical deci- sion analysis	Were all the clinically important strategies and outcomes included? Are the probabilities credible? Was the robustness of the conclusion tested?	Does one strategy result in a clinically important difference? How strong is the evidence used in analysis? How much does allowance for uncertainty change the results?			lysis?	Do the probability estimates approximate my patients' clinical features? If not can you adjust them properly? Do the utilities reflect my patients' values? Can they state their utilities in a stable and usable form?
Harm	Were there clearly defined groups of patients similar in all important ways other than exposure to the treatment? Were treatment exposures and clinical outcomes measured in the same way in both the groups? Was the follow-up of study patients complete and	Finding out if a treatment causes harm: calculate the strength of an association between a treatment and subsequent adverse outcomes. In RCT/cohort study: Relative risk = $[a/(a+b)]/[c/(c+d)]$ Case-control study: Relative odds = RO = ad/bc		eatment and (a+b)]/[c/(c+d)]	Can the study results be extrapolated to this patient? What are the patient's risks of the adverse outcome? What are the patient's preferences, concerns and expectations from this treatment? What alternative treatments are available?	
	long enough? Do the results satisfy some 'diagnostic tests for causation'?	Exposure	a b	sent	Totals a +b	
			c d a+c b+		c + d a + b + c + d	

Clinical prac- tice guideline	Were all important decision options and outcomes specified? Was the evidence relevant to each decision option identified, validated, and combined in a sensible and explicit way? Are the relative preferences the key stakeholders attach to the outcomes of decisions identified and explicitly considered? Is the guideline resistant to clinically sensible variations in practice?	Does the guideline offer an opportunity for significantly improving the quality of current health care practice? Is there a large variation in current clinical practice? Does the guideline contain new evidence that could positively impact clinical practice? Would the guideline significantly improve patient outcome?	Is the primary objective of the guidelines consistent with my goals? Are the recommendations applicable to my patients? What barriers exist to its implementation? Can they be overcome?
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Adapted from Sackett DL, Richardson WS, Rosenberg W, et al. Evidence-based medicine: How to practice & teach EBM. Edinburgh: Churchill Livingstone; 1998

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